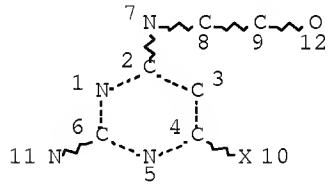
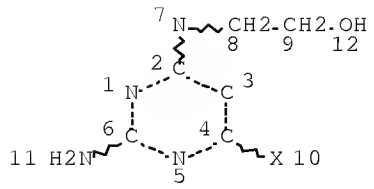
```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:28:45 ON 03 FEB 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 3 Feb 2010  VOL 152 ISS 6
FILE LAST UPDATED: 2 Feb 2010  (20100202/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Oct 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d stat que l6
L1              STR
```




```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L3          119 SEA FILE=REGISTRY SSS FUL L1
L4              STR
```



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

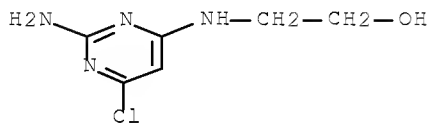
STEREO ATTRIBUTES: NONE
L5 8 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

=> d ibib abs hitstr l6 1-9

L6 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2005:526504 HCAPLUS Full-text
DOCUMENT NUMBER: 143:206671
TITLE: Gastrin-releasing peptide (GRP) induces angiogenesis and the specific GRP blocker 77427 inhibits tumor growth in vitro and in vivo
AUTHOR(S): Martinez, Alfredo; Zudaire, Enrique; Julian, Miguel; Moody, Terry W.; Cuttitta, Frank
CORPORATE SOURCE: Cell and Cancer Biology Branch and Vascular Biology Faculty, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Oncogene (2005), 24(25), 4106-4113
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiogenesis is becoming a major target for antitumor therapies, and identifying new angiogenic factors and their specific inhibitors may provide new avenues for tumor management. Here the authors identify gastrin-releasing peptide (GRP) as a new angiogenic mol. that is secreted by tumors and acts directly upon GRP receptors in the endothelial cells. Addition of GRP increases endothelial cell migration and cord formation in vitro, and induces angiogenesis in an in vivo assay. The authors have recently identified a small mol. GRP blocker, compound 77427. This inhibitor significantly reduced endothelial cell cord formation in vitro and angiogenesis in vivo. Conversely, when applied to VEGF-induced angiogenesis, the small mol. did not have any effect, demonstrating its specificity. Furthermore, this GRP blocker was able to reduce lung tumor cell growth in vitro as demonstrated by MTT and clonogenic assays. When applied to a xenograft model with lung cancer cells, compound 77427 reduced tumor volume to undetectable sizes, although when the treatment was suspended, tumors began to grow again at normal rates. The authors' collective observations indicate that GRP is a new angiogenic peptide and that its inhibition offers an attractive tool to reduce tumor burden.
IT 2846-77-7, NSC 77427
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrin-releasing peptide induction of angiogenesis and the specific GRP blocker compound 77427 inhibition of tumor growth in vitro and in vivo)

RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)

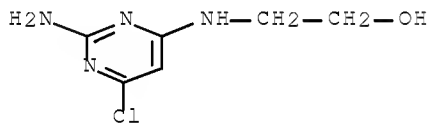


OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2005:260303 HCAPLUS Full-text
DOCUMENT NUMBER: 142:309954
TITLE: Non-peptide agonists and antagonists of adrenomedullin and gastrin-releasing peptide
INVENTOR(S): Cuttitta, Frank; Martinez, Alfredo
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026741	A2	20050324	WO 2004-US29293	20040908
WO 2005026741	A3	20050818		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273057	A2	20050324	AU 2004-273057	20040908
AU 2004273057	A1	20050324		
CA 2539467	A1	20050324	CA 2004-2539467	20040908
EP 1664798	A2	20060607	EP 2004-783513	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 20080249115	A1	20081009	US 2006-571012	20060308

PRIORITY APPLN. INFO.: US 2003-500650P P 20030908
US 2004-569625P P 20040511
WO 2004-US29293 W 20040908
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 142:309954
AB This invention relates, e.g., to methods for inhibiting or stimulating an activity of an adrenomedullin (AM) or gastrin releasing peptide (GRP) peptide hormone, comprising contacting the peptide with a small mol., non-peptide, modulatory agent of the invention. Complexes of these modulatory agents with other components, such as the peptides or blocking antibodies specific for the peptides, are also described, as are pharmaceutical compns. comprising the modulatory agents, and methods for using the modulatory agents to diagnose or treat patients.
IT 2846-77-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-peptide agonists and antagonists of adrenomedullin and gastrin-releasing peptide for treatment and diagnosis)
RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)

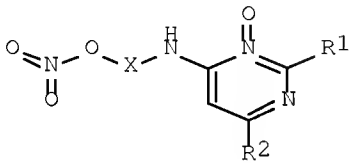


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

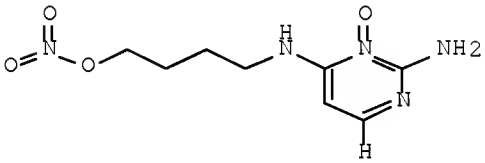
L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2004:960072 HCAPLUS Full-text
DOCUMENT NUMBER: 141:410943
TITLE: Preparation of pyrimidine N-oxide derivatives, and their hair compositions used to stimulate or induce the growth of hair and/or to slow down its loss
INVENTOR(S): Dalko, Maria; Mahe, Yann; Cals-Grierson, Marie-Madeleine
PATENT ASSIGNEE(S): L'Oreal, Fr.
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1475376	A1	20041110	EP 2003-292979	20031128
EP 1475376	B1	20070718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
FR 2854630	A1	20041112	FR 2003-50145	20030506
FR 2854630	B1	20050610		
AT 367385	T	20070815	AT 2003-292979	20031128
ES 2290415	T3	20080216	ES 2003-292979	20031128
JP 2004331664	A	20041125	JP 2004-137805	20040506

US 20050130991 A1 20050616 US 2004-839176 20040506
US 7326717 B2 20080205
PRIORITY APPLN. INFO.: FR 2003-50145 A 20030506
US 2003-507495P P 20031002
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 141:410943
GI



I

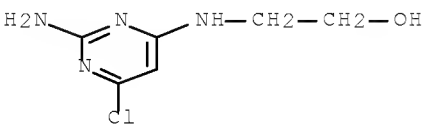


II

AB Title compds. I or one of its salts [wherein X = (CH2)n; n = 2-12; R1 = (un)substituted alkyl, or NH2 and derivs.; R2 = NR3R4, OR3, SR3; R3, R4 = independently (un)substituted alkyl; R3 and R4 can form a (un)saturated 4-7-membered ring cycle containing at least one heteroatom] were prepared as hair growth stimulant agents to reduce hair loss and to promote hair regrowth. For example, II was prepared in 4 steps, by amination of 2-amino-4,6-dichloropyrimidine with butanolamine, oxidation with H2O2 over Na2WO4 in MeOH/H2O to the N-oxide, dechlorination, and nitration of the alc. with fuming HNO3. Selected I were NO donors and lysyl-hydroxylase inhibitors. Thus, I are useful in cosmetic and pharmaceutical compns. used to stimulate hair and eyelashes growth and/or slowing down their loss.

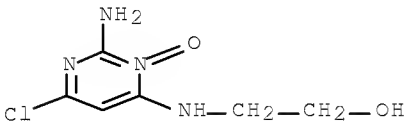
IT 2846-77-7P 791097-22-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrimidine N-oxide derivs., and their hair compns. used to stimulate or induce growth of hair and/or to slow down its loss)

RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



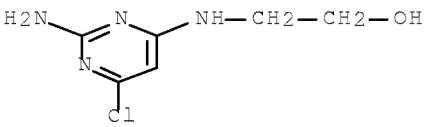
RN 791097-22-8 HCAPLUS

CN Ethanol, 2-[(2-amino-6-chloro-3-oxido-4-pyrimidinyl)amino]- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:598995 HCAPLUS Full-text
DOCUMENT NUMBER: 130:3819
TITLE: Specific inhibitors in vitamin biosynthesis. Part 10. Synthesis of 7- and 8-substituted 7-deazaguanines
AUTHOR(S): Gibson, Colin L.; Ohta, Kyuji; Paulini, Klaus; Suckling, Colin J.
CORPORATE SOURCE: Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, G1 1XL, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1998), (18), 3025-3032
CODEN: JCPRB4; ISSN: 0300-922X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:3819
AB Versatile syntheses of 7- and 8-substituted 7-deazaguanines including N-alkyl derivs. have been developed by identifying selective annulation reactions with 2,6-diaminopyrimidin-4(3H)-one as substrate and β-halocarbonyl compds. as electrophiles. A new synthesis of 8-substituted 7-deazaguanines using nitrosoalkenes as electrophiles is described. With some combinations of reactants, furo[2,3-d]pyrimidines are significant products in place of or in addition to the required 7-deazaguanines [pyrrolo[2,3-d]pyrimidin-4(3H)-ones]. When 2,4-diamino-6-chloropyrimidine was used as a substrate, imidazopyrimidines were produced.
IT 2846-77-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 7- and 8-substituted 7-deazaguanines)
RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



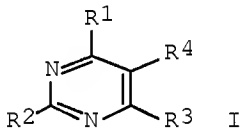
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD

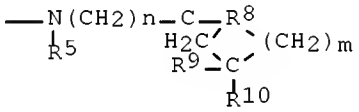
(7 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

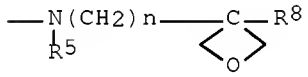
L6 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:512446 HCAPLUS Full-text
DOCUMENT NUMBER: 129:211709
ORIGINAL REFERENCE NO.: 129:42843a,42846a
TITLE: Antitumor agents containing pyrimidine derivatives
INVENTOR(S): Hisaki, Masakatsu; Ota, Yoichiro; Kawanishi, Kenji; Bonshihara, Yasuko; Iwakura, Fudzuki; Tomio, Kaoru; Node, Satoru; Nishiide, Kiyoji
PATENT ASSIGNEE(S): Nippon Shoji Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 28 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

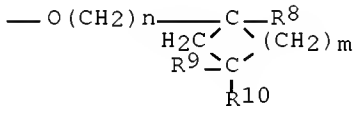
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10212235	A	19980811	JP 1997-15628	19970129

PRIORITY APPLN. INFO.: JP 1997-15628 19970129
OTHER SOURCE(S): MARPAT 129:211709
GI


I


II


III

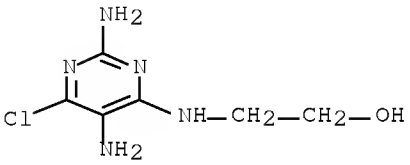

IV

AB The antitumor agents contain pyrimidine derivs. I [R1 = H, C1-4 alkyl, halo, OH, C1-4 alkoxy, C1-6 hydroxyalkoxy, NH3; R2 = NH2, NHAc; R3 = NR5(CH2)iCH2OH, NR5(CH2)nCR6R7R8, II, III, IV; R4 = H, halo, NH2, cyano, CHO, CH2OH, CO2H, CH2NH2, CONH2, CH:NA (A = OH, C1-4 alkyl, C1-4 alkoxy), N:NZ (Z = aryl which may be substituted with C1-4 alkyl, halo, NO2, C1-4 alkoxy); R5 = H, C1-4 alkyl; R6, R7 = C1-4 alkyl; R8 = H, OH, C1-4 hydroxyalkyl, CH2OAc; R9 = H, OH, C1-4 alkyl, C1-4 hydroxyalkyl, C1-4 alkoxy, vinyl, O(CH2)kR (R = aryl which may be substituted with C1-4 alkyl, halo, C1-4 alkoxy; k = 0-4), (CH2)jR11 (R11 = OBz, aryl which may be substituted with C1-4 alkyl, halo, C1-4 alkoxy; j = 0-6); R10 = H, OH, C1-4 alkoxy; CR9R10 may be C:CH2, CO; cycloalkyl ring of II and IV may have double bond; i = 1-4; n, m = 0-4; except the case when n = 0 and R8 = H] or their pharmacol. acceptable salts as active ingredients. In vitro antitumor activity of 2-amino-6-chloro-5-[(4-chlorophenyl)azo]-4-[[(1- hydroxymethyl-3-phenylmethyloxy-1-cyclobutyl)methyl]amino]pyrimidine (preparation given) against various leukemia,

melanoma, lung cancer, mammary cancer, colonic cancer, cerebral cancer, ovary cancer, and renal cancer cell lines were shown. Toxicity of I were also examined Capsules of I were also formulated.

IT 199453-10-6P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. as antitumor agents)

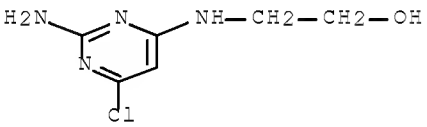
RN 199453-10-6 HCAPLUS
CN Ethanol, 2-[(2,5-diamino-6-chloro-4-pyrimidinyl)amino]-, hydrochloride (1:2) (CA INDEX NAME)



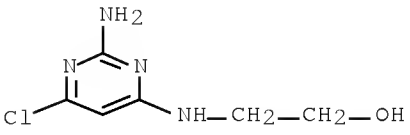
●2 HCl

IT 2846-77-7P 199453-05-9P 199453-09-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. as antitumor agents)

RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



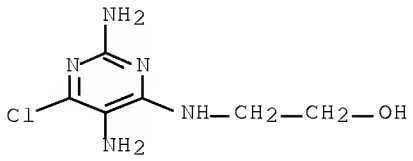
RN 199453-05-9 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 199453-09-3 HCAPLUS

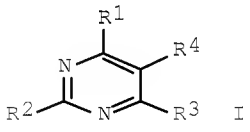
CN Ethanol, 2-[(2,5-diamino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



L6 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:743999 HCAPLUS Full-text
DOCUMENT NUMBER: 128:22917
ORIGINAL REFERENCE NO.: 128:4495a,4498a
TITLE: Preparation of pyrimidine compounds as anti-rotavirus agents
INVENTOR(S): Hisaki, Masakatsu; Ohta, Yoichiro; Kawanishi, Kenji; Ichigobara, Yasuko; Iwakura, Fuzuki; Azuma, Masanobu; Suzutani, Tatsuo; Node, Manabu; Nishide, Kiyoharu
PATENT ASSIGNEE(S): Nippon Shoji Kaisha Ltd., Japan
SOURCE: Eur. Pat. Appl., 63 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 806418	A2	19971112	EP 1997-107647	19970509
EP 806418	A3	19971203		
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, FI				
JP 09301958	A	19971125	JP 1996-115147	19960509
US 6080750	A	20000627	US 1997-852118	19970506
PRIORITY APPLN. INFO.:			JP 1996-115147 A	19960509

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 128:22917
GI

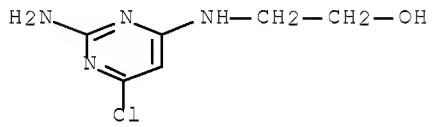


AB Pyrimidine compds. of the formula [I; R1 = H, C1-4 lower alkyl, halogen atom, OH, C1-4 lower alkoxy, C1-6 hydroxy-lower alkoxy or NH2 ; R2 = H, NH2, or NHCOCH3; R3 = NR5(CH2)iCH2OH; R4 = H, halogen atom, NH2, cyano, CHO, -CH2H, CO2H, CH2NH2, CONH2 or CH:N-A wherein A is OH, C1-4 lower alkyl or C1-4 lower alkoxy; R5 = H or C1-4 lower alkyl; i = an integer of 1 to 4] are prepared An anti-rotavirus agent comprising, as an active ingredient, a compound of the formula I is claimed. These pyrimidine compds. of the present invention and related derivs. thereof have superior anti-rotavirus action and are useful for the prophylaxis and treatment of rotaviral

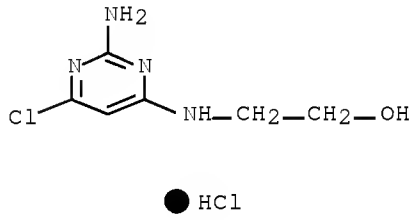
diseases such as infant diarrhea (white diarrhea) and acute gastroenteritis. Thus, to hydroxyethylamine were added 2-amino-4,6-dichloropyrimidine, EtOH, and Et3N and the mixture was refluxed for 1 day to give 59.6% I (R1 = Cl, R2 = NH2, R3 = NHCH2CH2OH, R4 = H). The most active title compound I (R1 = Cl, R2 = R4 = NH2, R3 = NHCH2CEt2CH2OH) showed ID50 (50% plaque inhibition dose) of 0.2 μg/mL for CV-1 cells infected with rotavirus SA-11 strain. It showed the least cytotoxicity with ED50 (50% cell growth inhibition effect) of 30.0 μg/mL against host CV-1 cells.

IT 2846-77-7P 199453-05-9P 199453-09-3P
199453-10-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine compds. as anti-rotavirus agents)

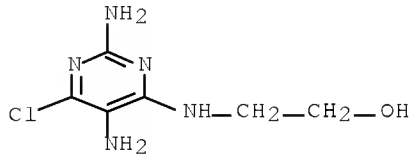
RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



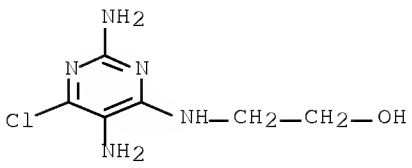
RN 199453-05-9 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



RN 199453-09-3 HCAPLUS
CN Ethanol, 2-[(2,5-diamino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)

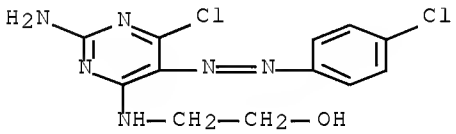


RN 199453-10-6 HCAPLUS
CN Ethanol, 2-[(2,5-diamino-6-chloro-4-pyrimidinyl)amino]-, hydrochloride (1:2) (CA INDEX NAME)



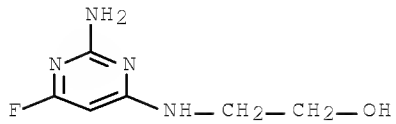
●2 HCl

IT 2846-78-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidine compds. as anti-rotavirus agents)
RN 2846-78-8 HCAPLUS
CN Ethanol, 2-[[2-amino-6-chloro-5-[2-(4-chlorophenyl)diazenyl]-4-pyrimidinyl]amino]- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:266069 HCAPLUS Full-text
DOCUMENT NUMBER: 126:277444
ORIGINAL REFERENCE NO.: 126:53787a,53790a
TITLE: Synthesis and properties of 2,4-disubstituted 6-fluoropyrimidines
AUTHOR(S): Popova, L. M.; Studentsov, E. P.
CORPORATE SOURCE: St. Petersburg. Gos. Tekhnol. Inst., St. Petersburg, 198013, Russia
SOURCE: Zhurnal Organicheskoi Khimii (1996), 32(9), 1424-1428
CODEN: ZORKAE; ISSN: 0514-7492
PUBLISHER: Nauka
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 126:277444
AB Reaction of 2,4,6-trifluoropyrimidine, 2-amino-4,6-difluoropyrimidine, and 4-amino-2,6-difluoropyrimidine with amines gave fluoropyrimidines containing two like or unlike amino groups.
IT 188987-84-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 188987-84-0 HCAPLUS
CN Ethanol, 2-[(2-amino-6-fluoro-4-pyrimidinyl)amino]- (CA INDEX NAME)



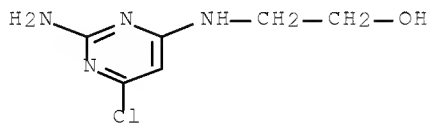
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L6 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1965:58932 HCAPLUS Full-text
DOCUMENT NUMBER: 62:58932
ORIGINAL REFERENCE NO.: 62:10435f-g
TITLE: Synthesis and antitumor activity of 9-substituted nitrogen mustard derivatives of 6-alkylthiopurines
AUTHOR(S): O'Brien, Darrell E.; Westover, James D.; Robins, Roland K.; Cheng, C. C.
CORPORATE SOURCE: Midwest Res. Inst., Kansas City, MO
SOURCE: Journal of Medicinal Chemistry (1965), 8(2), 182-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 62:58932

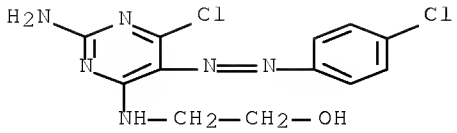
AB The preparation of 6-alkylthio-9-(β-chloroethyl)purines and 6-alkylthio-9-[bis(β-chloroethyl)aminoethyl]purines was reported. Direct alkylation of 6-(alkylthio)purines with ethylene bromohydrin or 2-bromoethyl chloride in Me2SO gave 6-(alkylthio)-9-(β-hydroxyethyl)purines or 6-(alkylthio)-9-(β-chloroethyl)purines, resp., in good yield. These compds. were identical with those prepared by alternate and unambiguous synthetic routes. Although cyclization of some 4-(β-chloroethylamino)pyrimidines to dihydroimidazolo[2,3-c]pyrimidines has been reported, the closely related 2-amino-6-alkylthio-9-(β-chloroethyl)purines did not undergo a similar type cyclization. Several 6-alkylthio-9-(β-hydroxyethyl)- and -9-(β-chloroethyl)purines possess antitumor activity against Adenocarcinoma 755 system. In addition, significant activities in Friend virus leukemia (solid) and in tissue culture studies have also been observed in some 6-(aralkylthio)-9-(β-chloroethyl)purines. Cf. Clark and Ramage, CA 52, 2018d.

IT 2846-77-7P, Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]-
2846-78-8P, Ethanol, 2-[[2-amino-6-chloro-5-[(p-chlorophenyl)azo]-4-pyrimidinyl]amino]-
RL: PREP (Preparation)
(preparation of)

RN 2846-77-7 HCAPLUS
CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



RN 2846-78-8 HCAPLUS
CN Ethanol, 2-[[2-amino-6-chloro-5-[2-(4-chlorophenyl)diazenyl]-4-pyrimidinyl]amino]- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1962:25089 HCAPLUS Full-text
DOCUMENT NUMBER: 56:25089
ORIGINAL REFERENCE NO.: 56:4752b-i,4753a-h
TITLE: Pteridines. XV. Synthesis of 2-amino-4-alkoxy-7-oxodihydropteridines
AUTHOR(S): Pficiderer, Wolfgang; Lohrmann, Rolf
CORPORATE SOURCE: Tech. Hochschule, Stuttgart, Germany
SOURCE: Chemische Berichte (1961), 94, 2708-21
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 56:25089

AB cf. CA 55, 551g, 10462f.-The synthesis of 2-amino-4-alkoxy-7-oxodihydropteridine derivs. was described and their structure discussed on the basis of the ultraviolet absorption spectra. 4,6-Dichloro-2-aminopyrimidine (I) (50 g.) in 220 g. 10% MeNH2 in PrOH kept at room temperature overnight, warmed slowly, heated 2 hrs. on the water bath, evaporated, the residue dissolved in about 350 cc. hot H2O, the solution treated with C, filtered, and cooled slowly gave 40 g. 6-chloro-2-amino-4-methyl-aminopyrimidine (II), m. 162-4° (H2O). I (60 g.), 120 cc. 33% aqueous MeNH2, and 300 cc. 2:1 MeOH-H2O stirred 4 hrs. at 60-80°, filtered hot, and cooled gave 36 g. crude II. I (50 g.) in 200 cc. EtOH refluxed 3 hrs. with 45 g. H2NCH2CH2OH and worked up in the usual manner gave 47 g. 4-(HOCH2CH2NH) analog (III) of II, m. 149-51° (H2O). I (40 g.) refluxed 2.5 hrs. with 6.2 g. Na in 300 cc. iso-PrOH, concd, in vacuo to 80°, acidified with dilute AcOH, and cooled gave 45 g. 4-chloro-2-amino-6-isopropoxypyrimidine (IV), needles, m. 85-6° (aqueous MeOH). II (70 g.) heated 8 hrs. at 150-60° in an autoclave with 11.2 g. Ha in 700 cc. isoPrOH, filtered hot, concd, in vacuo, and diluted with a little xylene gave 71 g. 4-MeNH analog (V) of IV, m. 105-7° (CCl4-petr. ether). II (60 g.) and 9.6 g. Na in 600 cc. MeOH gave similarly 57 g. 6-MeO analog (VI) of V, m. 135-7° (xylene). V (53 g.) in 500 cc. 10% AcOH treated dropwise with stirring at 40° with 22 g. NaNO2 in about 30 cc. H2O, the mixture neutralized with solid NaHCO2, cooled, and filtered gave 41 g. 5-NO derivative (VII) of V, violet, m. 180-1° (decomposition) (xylene). VI (55 g.) in 150 cc. 15% AcOH treated dropwise with stirring at 70-80° with 28 g. NaNO2 gave similarly 46 g. 5-NO derivative (VIII) of VI, violet needles, m. 210-11° (H2O). III (10 g.) heated 7 hrs. in an autoclave at 140-50° with 1.4 g. Na in 200 cc. iso-PrOH, neutralized with AcOH, filtered, evaporated in vacuo, the residue treated with aqueous NANO2 at 50-60°, and the product isolated with CHCl3 yielded the violet 5-NO derivative (IX) of III, m. 150-8° (CHCl3-CCl4). VII (15 g.) in 200 cc. MeOH hydrogenated over Raney Ni yielded 13.8 g. light yellow 5-NH2 derivative (X) of V, m. 96-8° (ligroine). VIII (15 g.) gave similarly 13.1 g. 5-NH2 derivative of VI, needles, m. 171-3° (xylene). 2,4,5-Triamino-6-isopropoxypyrimidine (XI) (2 g.) in 80 cc. MeOH refluxed 4 hrs. with 1.8 g. EtO(HO)CHCO2Et (XII), concentrated to half-volume, and refrigerated 12 hrs. yielded 1.4 g. 2-amino-4-isopropoxy-7-

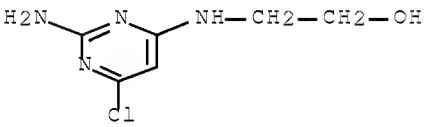
oxodihydropteridine (XIII), m. above 360° (PhCH2OH). 5-Nitroso-2,4-diamino-6-isopropoxypyrimidine (6 g.) in 200 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 2 hrs. with 4.8 g. BzCO2Et, and refrigerated overnight gave 6.7 g. 6-Me derivative (XIV) of XIII, m. above 360° (PhCH2OH). XI (2 g.) in 80 cc. 50% MeOH refluxed 2.5 hrs. with 2.1 g. CO(CO2Et)2 (XV) gave 1.0 g. 6CO2Et analog (XVI) of XIV, m. above 320° (decomposition). XVI (1 g.) in 150 cc. 0.6M NaHCO3 heated 4 hrs. on the water bath, filtered, acidified hot with 50% AcOH, and kept overnight yielded 0.64 g. 6-CO2H analog (XVII) of XIV, m. above 360° (aqueous HCONMe2). VIII (2.5 g.) in 150 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 2 hrs. with 2.3 g. XII, concentrated, and kept overnight gave 2.1 g. 8-methyl-2-amino-4-methoxy-7-oxodihydropteridine (XVIII), light yellow needles, m. 262-6° (decomposition) (aqueous EtOH). VIII (2.5 g.) in 150 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 2 hrs. with 2 g. BzCO2Et, and concentrated gave 2.2 g. 6-Me derivative (XIX) of XVIII, m. 258-62° (decomposition) (aqueous EtOH). VIII (5 g.) in 200 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 5 hrs. with 5 g. XV, and concd, gave 6.5 g. 6-CO2Et analog (XX) of XIX, yellow, m. 254-7° (decomposition) (CHCl3-petr. ether). XX (3.4 g.) in 300 cc. N NaHCO2 heated 2 hrs. on the water bath, filtered hot, acidified with AcOH, concentrated, and cooled yielded 2 g. 6-CO2H analog (XXI) of XIX, yellow, m. 252-4° (decomposition) (aqueous HCONMe2). VII (2.5 g.) in 150 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 1.5 hrs. with 1.9 g. XII, concentrated in vacuo to 15 cc., diluted with 40 cc. xylene, treated with C, concentrated to about 15 cc., and cooled overnight gave 0.35 g. light yellow 8-Me derivative (XXII) of XVI, m. 232-4° (ligroine). X (1 g.) and 0.7 g. BzCO2Et in 50 cc. MeOH refluxed 0.5 hr., poured into 150 cc. hot H2O, and cooled gave 0.9 g. 6-Me derivative (XXIII) of XXII, cream needles, m. 243-5° (aqueous EtOH). VII (5 g.) in MeOH hydrogenated over Raney Ni, filtered, treated with 5 g. XV, the mixture concentrated to half volume, diluted with 25 cc. H2O, refluxed 1 hr., and cooled yielded 4.8 g. 6-CO2Et derivative (XXIV) of XXII, m. 192-4° (ligroine). XXIV (4 g.) in 200 cc. N NaHCO3 heated 2 hrs. on the water bath, cooled, acidified with 40 cc. 50% AcOH, and cooled to 0° gave 3.5 g. crude product, which extracted with CHCl3 and recrystd. from aqueous HCONMe2 gave the 6CO2H derivative (XXV) of XXII, light yellow needles, m. 246-7° (decomposition). IX (1.8 g.) in 150 cc. MeOH hydrogenated over Raney Ni, filtered, refluxed 1 hr. with 2.5 cc. BzCO2Et, concentrated to 20 cc., and cooled yielded 1.25 g. 8-(2-hydroxyethyl)-2-amino-4-isopropoxy-6-methyl- 7-oxodihydropteridine (XXVI), m. 229-31° (aqueous EtOH). XI (2 g.) in 25 cc. (CO2Et)2 heated 10-15 min. at 160-80° gave 2.3 g. 2-amino-4-isopropoxy-6, 7-dioxotetrahydropteridine (XXVII), pale yellow, m. above 360° (4:1 glycol-H2O). X (2.5 g.) in 25 cc. (CO2Et)2 heated slowly to 180°, kept 15 min. at 180°, cooled, and filtered yielded 2.7 g. (crude) 8-Me derivative (XXVIII) of XXVII, m. 244-7° (decomposition) (ligroine). 5-Nitroso-2,4-diamino-6-isopropoxypyrimidine (XXIX) in 40 cc. NCCH2CO2Me heated to near boiling, cooled after 10 min., and filtered gave 1.4 g. 6-CN derivative (XXX) of XIII, yellowish, decomposed above 250° (HCONMe2). XXIX (2 g.) and 4 g. CH2(CN)2 in 20 cc. EtOCH2CH2OH heated slowly to 120-30°, cooled slightly after 15 min., poured into hot H2O, kept several hrs., and filtered yielded 1.1 g. 2,7-diamino-4-isopropoxy-6-cyanopteridine (XXXI), decomposed above 220° (aqueous EtOH). The ultraviolet absorption spectra of the neutral mols. and cations of XVI, XVII, XXIV, XXV, and XXX were recorded. The Rf in 2:1 BuOH-5N AcOH, PrOH-1% NH3, 4% aqueous Na citrate, and 3% aqueous NH4Cl (given in this order) and the pK values in H2O at 20° at the pH indicated in parentheses were determined for the following compds.: XIII, 0.67, 0.55, 0.39, 0.45, 0.74 ± 0.16 (-1.9), 7.60 ± 0.2 (5.0); XIV, 0.68, 0.56, 0.38, 0.42, 1.14 ± 0.13 (-0.89), 7.8 ± 0.2 (5.0); XXII, 0.84, 0.82, 0.52, 0.60, 0.17 ± 0.15 (-1.9); XXIII, 0.86, 0.85, 0.52, 0.56, 0.40 ± 0.18 (-1.9); XVIII, 0.61, 0.66, 0.36, 0.40, 0.21 ± 0.08 (-1.9); XIX, 0.69, 0.72, 0.42, 0.43, 0.55 ± 0.2 (-1.9); XXVI, 0.83, 0.87, 0.63, 0.63, 0.74 ± 0.1 (-1.9): XVII, 0.42, 0.27, 0.62, 0.59, 0.35 ± 0.13

(-1.9), 3.71 ± 0.11 (2.0), 8.32 ± 0.06 (6.0); XVI, 0.75, 0.62, 0.49, 0.53, 0.35 ± 0.12 (-1.9), 7.8 ± 0.2 (3.0); XXV, 0.65, 0.50, 0.71, 0.75, -0.76 ± 0.12 (-2.7), 3.53 ± 0.08 (1.0); XXIV, 0.83, 0.85, 0.62, 0.64, -0.46 ± 0.08 (-2.7); XXI, 0.32, 0.28, 0.55, 0.63, -0.4 ± 0.1 (-2.7), 3.86 ± 0.13 (1.0); XX, 0.69, 0.74, 0.53, 0.54, -0.60 ± 0.1 (-2.7); XXX, 0.72, 0.56, 0.28, 0.38, -0.17 ± 0.08 (-1.9), 5.95 ± 0.13 (4.0); XXXI, 0.69, 0.71, 0.26, 0.29, 41.0 ± 0.13 (2.0); XXVII, 0.50, 0.32, 0.40, 0.45, 0.82 ± 0.07 (-1.9), 8.46 ± 0.14 (4.0), 12.2 ± 0.2 (10.0); XXVIII, 0.73, 0.62, 0.52, 0.60, 0.53 ± 0.11 (-1.9), 8.53 ± 0.09 (6.0); 1,3,6-trimethyl-7-hydroxy-2,4-dioxotetrahydropteridine, 0.70, 0.50, 0.50, 0.60, -. The various dihydropteridine derivs. showed at 254 and 365 mμ blue fluorescence, while XXVII and XXVIII fluoresced gray except in 4% aqueous Na citrate where the fluorescence was also blue.

IT 2846-77-7P, Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]-
RL: PREP (Preparation)
(preparation of)

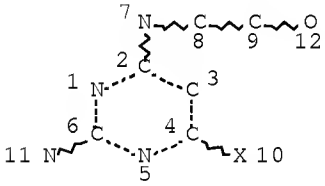
RN 2846-77-7 HCAPLUS

CN Ethanol, 2-[(2-amino-6-chloro-4-pyrimidinyl)amino]- (CA INDEX NAME)



=> => d stat que l16

L1 STR



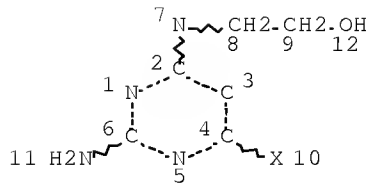
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L3 119 SEA FILE=REGISTRY SSS FUL L1

L4 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L5 8 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L7 233 SEA FILE=HCAPLUS ABB=ON PLU=ON ("CUTTITTA F"/AU OR "CUTTITTA F F"/AU OR "CUTTITTA FRANCK"/AU OR "CUTTITTA FRANK"/AU OR "CUTTITTA FRANK C"/AU OR "CUTTITTA FRANK F JR"/AU OR "CUTTITTA FRANKLIN"/AU)
L8 1986 SEA FILE=HCAPLUS ABB=ON PLU=ON ("MARTINEZ ALFREDO"/AU OR "MARTINEZ ALFREDO CORDOVA"/AU OR "MARTINEZ ALFREDO J"/AU OR "MARTINEZ ALFREDO LORENZO LUACE"/AU OR "MARTINEZ ALFREDO ORDEN"/AU) OR MARTINEZ A/AU OR MARTINEZ A ?/AU
L11 93 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND L8
L14 82 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND (?ADRENO? OR ?GAST?)
L15 67 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND (AY=<2003 OR PY=<2003 OR PRY=<2003 OR PD=<OCTOBER 8, 2003)
L16 66 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L6

=> d ibib abs hitstr l16 1-66

L16 ANSWER 1 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2004:430708 HCAPLUS Full-text
DOCUMENT NUMBER: 141:1253
TITLE: Use of proadrenomedullin peptide in regulating angiogenesis
INVENTOR(S): Cuttitta, Frank; Martinez, Alfredo; Stetler-Stevenson, William G.
PATENT ASSIGNEE(S): The Government of the United States of America as Represented by the Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043383	A2	20040527	WO 2003-US35633	20031107 <--
WO 2004043383	A3	20060223		

```
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
            NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
            TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    CA 2504953          A1    20040527    CA 2003-2504953        20031107 <--
    AU 2003295422       A1    20040603    AU 2003-295422         20031107 <--
    AU 2003295422       B2    20090129
    EP 1575511          A2    20050921    EP 2003-786608         20031107 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    JP 2006516537       T     20060706    JP 2004-551922         20031107 <--
    US 20060160730      A1    20060720    US 2005-529116         20050324 <--
    US 7462593          B2    20081209
    US 20090048170      A1    20090219    US 2008-240656         20080929 <--
PRIORITY APPLN. INFO.:                      US 2002-425018P     P  20021107 <--
                                            WO 2003-US35633     W  20031107 <--
                                            US 2005-529116      A3 20050324
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB    The present disclosure concerns the use of proadrenomedullin peptide in promoting
or inhibiting angiogenesis.  Angiogenic potential of basic fibroblast growth factor,
vascular endothelial growth factor, proadrenomedullin and adrenomedullin are compared.
OS.CITING REF COUNT:     2     THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
                               (2 CITINGS)
REFERENCE COUNT:         1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16  ANSWER 2 OF 66  HCAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2004:331893  HCAPLUS  Full-text
DOCUMENT NUMBER:         140:350576
TITLE:                   Vasoregulating peptides derived in vivo from human
                         adrenomedullin and their therapeutic use
INVENTOR(S):             Cuttitta, Frank; Martinez, Alfredo;
                         Stetler-Stevenson, William G.; Unsworth, Edward J.;
                         Saavedra, Juan M.
PATENT ASSIGNEE(S):      United States Dept. of Health and Human Services, USA
SOURCE:                  PCT Int. Appl., 40 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------          ----   --------    -------------------    --------
     WO 2004032708       A2     20040422    WO 2003-US31400        20031003 <--
     WO 2004032708       A3     20040715
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
```

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2501282	A1	20040422	CA 2003-2501282	20031003 <--
AU 2003282660	A1	20040504	AU 2003-282660	20031003 <--
AU 2003282660	B2	20080918		
US 20050261179	A1	20051124	US 2005-529118	20050324 <--
US 7364719	B2	20080429		

PRIORITY APPLN. INFO.: US 2002-416291P P 20021004 <--
WO 2003-US31400 W 20031003 <--

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods and compds. are described for regulating blood pressure in a subject. Specific embodiments are methods for reversing vasodilation of blood vessels, by administering to a subject a therapeutically effective amount peptide AM(11-22), comprising residues 11-22 of human adrenomedullin (residues 105-116 of the preproadrenomedullin, GenBank NP_001115). Adrenomedullin is specifically degraded by matrix metalloproteinase-2 (MMP-2), producing specific adrenomedullin digestion products that can be detected in the urine of normal individuals. Vasoconstrictor activity of AM(11-22) in rats occurs without the peptide interacting with CRLR, RAMP2, or RAMP3 (the expected receptor components), suggesting that other independent receptor system(s) may be involved in the observed vasoconstrictor activity. Hypotensive and hypertensive adrenomedullin peptides exhibit very different modes of action, with the vasodilator mols. acting almost immediately following injection, and the vasoconstrictor peptide needing 4-5 min before eliciting its effect. The vasoconstrictor can be used for a variety of purposes, including hemostasis or the treatment of shock, for example vasodilatory shock syndromes such as septic shock. Other specific embodiments are methods for reversing vasoconstriction of blood vessels, by administering to a subject a therapeutically effect amount of an inhibitor of AM(11-22), sufficient to reduce hypertension in the subject.

L16 ANSWER 3 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2003:246196 HCAPLUS Full-text
DOCUMENT NUMBER:	139:51363
TITLE:	Mapping of the adrenomedullin-binding domains in human complement factor H
AUTHOR(S):	Martinez, Alfredo; Pio, Ruben; Zipfel, Peter F.; Cuttitta, Frank
CORPORATE SOURCE:	Cell and Cancer Biology Branch, Vascular Biology Faculty, National Cancer Institute, NIH, Bethesda, USA
SOURCE:	Hypertension Research (2003), 26(Suppl.), S55-S59 CODEN: HRESE4; ISSN: 0916-9636
PUBLISHER:	Japanese Society of Hypertension
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Adrenomedullin (AM) is a multifunctional peptide involved in roles as varied as blood pressure regulation, growth, neurotransmission, and inflammation control, among others. The authors previously identified complement factor H as a serum binding protein for AM and showed that factor H regulates AM functions and vice versa. Here the authors searched for the specific binding sites for AM by using recombinant fragments of factor H and a non-radioactive binding assay with fluorescein-tagged AM. By this methodol., two specific binding sites for AM were found in factor H. One of them shows a high affinity for AM and is located at the C-terminal end of factor H, comprising short consensus repeats (SCR) 15-20. Smaller fragments of this region did not bind to AM efficiently, suggesting that the high affinity binding site of factor H requires a complex three-dimensional structure to

recognize AM. Another binding site with lower affinity for AM was found in the middle of the factor H mol., at SCR 8-11. Antibodies against factor H prevented AM binding altogether, but the main binding partner of factor H, C3b, did not, indicating that C3b and AM bind to different regions of factor H. These structure-function data support previous biochem. observations. The authors' understanding of the binding between AM and factor H may help in the development of new treatments for diseases in which these mols. play active roles.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:231886 HCAPLUS Full-text
DOCUMENT NUMBER: 139:34026
TITLE: Adrenomedullin and cancer
AUTHOR(S): Zudaire, E.; Martinez, A.; Cuttitta, F.
CORPORATE SOURCE: Cell and Cancer Biology Branch, National Institutes of Health, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Regulatory Peptides (2003), 112(1-3), 175-183
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a pluripotent hormone with structural similarities to calcitonin gene-related peptide (CGRP), which is expressed by many tissues in the body and shows a remarkable range of effects mediated by paracrine/autocrine and possibly endocrine mechanisms. AM has been implicated as a mediator of several pathologies such as cardiovascular and renal disorders, sepsis, inflammation, diabetes and cancer, among others. AM is expressed in a variety of tumors where it aggravates several of the mol. and physiol. features of malignant cells. AM has been shown to be a mitogenic factor stimulating growth in several cancer types and to encourage a more aggressive tumor phenotype. In addition, AM is an apoptosis survival factor for cancer cells and an indirect suppressor of the immune response through its binding protein, complement factor H, and regulation in expression of cytokines. AM plays an important role in environments subjected to low oxygen tensions, which is a typical feature in the proximity of solid tumors. Under these conditions, AM is upregulated through a hypoxia-inducible factor 1 (HIF-1)-dependent pathway and acts as a potent angiogenic factor promoting neovascularization. The collective findings brought together over the last years place AM as a major regulator of carcinogenesis-tumor progression and identifies its autocrine loop as a putative target for developing new strategies against human cancers. OS.CITING REF COUNT: 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)
REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:231879 HCAPLUS Full-text
DOCUMENT NUMBER: 139:79204
TITLE: Regulation of pancreatic physiology by adrenomedullin and its binding protein
AUTHOR(S): Zudaire, E.; Cuttitta, F.; Martinez, A.
CORPORATE SOURCE: Department of Cell and Cancer Biology, National Institutes of Health, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Regulatory Peptides (2003), 112(1-3), 121-130
CODEN: REPPDY; ISSN: 0167-0115

PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a 52 amino acid, multifunctional hormone. It is expressed in many tissues of the human body including the pancreas, where it is mainly localized to the periphery of the islets of Langerhans and specifically to the pancreatic polypeptide-expressing cells. The AM receptor, a complex formed by calcitonin receptor-like receptor (CRLR) and receptor activity-modifying proteins (RAMPs), and the recently discovered AM-binding protein, complement factor H (fH), are expressed in the insulin-producing β-cells. The colocalization of these key elements of the AM system in the endocrine portion of the pancreas implicates AM in the control of both normal and altered pancreatic physiologies. AM inhibits insulin secretion both in vitro (isolated rat islets) and in vivo (oral glucose tolerance test in rats) in a dose-dependent manner. The addition of fH to isolated rat islets produces a further reduction of insulin secretion in the presence of AM. Furthermore, AM is elevated in plasma from patients with pancreatic dysfunctions such as type 1 or type 2 diabetes and insulinoma. Using a diabetic model in rats, the authors have shown that AM increases circulating glucose levels, whereas a blocking monoclonal antibody against AM has the opposite effect and improves postprandial recovery. Such exptl. evidence implicates AM as a fundamental factor in maintaining insulin homeostasis and normoglycemia, and suggests the implication of AM as a possible causal agent in diabetes. Further investigation focused on the development of blocking agents for AM could result in new treatments for pancreatic AM-related disorders. OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS
RECORD (10 CITINGS)
REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:166216 HCAPLUS Full-text
DOCUMENT NUMBER: 138:396586
TITLE: Distribution of immunoreactivity for the adrenomedullin binding protein, complement factor H, in the rat brain
AUTHOR(S): Serrano, J.; Encinas, J. M.; Fernandez, A. P.; Castro-Blanco, S.; Alonso, D.; Fernandez-Vizarra, P.; Richart, A.; Bentura, M. L.; Santacana, M.; Cuttitta, F.; Martinez, A.; Rodrigo, J.
CORPORATE SOURCE: Department of Neuroanatomy and Cell Biology, Cajal Institute, CSIC, Madrid, E-28002, Spain
SOURCE: Neuroscience (Oxford, United Kingdom) (2003), 116(4), 947-962
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An adrenomedullin-binding protein has recently been found in plasma and characterized as complement factor H. This regulator of the complement system inhibits the progression of the complement cascade and modulates the function of adrenomedullin. Our study shows the ample distribution of factor H immunoreactivity in neurons of telencephalon, diencephalon, mesencephalon, pons, medulla, and cerebellum in the rat CNS, using immunohistochem. techniques for both light and electron microscopy. Factor H immunoreactivity was found in the cytoplasm, but nuclear staining was also a common finding. Some blood vessels and glial cells were also immunoreactive for factor H. Colocalization studies by double immunofluorescence followed by confocal microscopy revealed frequent coexistence of factor H and adrenomedullin immunoreactivities, thus providing morphol. evidence for the potential interaction of these mols. in the CNS. The

presence of factor H immunoreactivity in glial cells was confirmed by colocalization with glial fibrillary acidic protein. In summary, factor H is highly expressed in the CNS where it could play important roles in regulating adrenomedullin actions and contributing to an intracerebral complement system. OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD
(7 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:937825 HCAPLUS Full-text
DOCUMENT NUMBER: 139:194603
TITLE: Distribution and possible function of an adrenomedullin-like peptide in the developing chick limb bud
AUTHOR(S): Reza Seghatoleslami, M.; Martinez, Alfredo; Cuttitta, Frank; Kosher, Robert A.
CORPORATE SOURCE: University Connecticut Health Center, Farmington, CT, USA
SOURCE: International Journal of Developmental Biology (2002), 46(7, Spec.), 957-961
CODEN: IJDBE5; ISSN: 0214-6282
PUBLISHER: University of the Basque Country Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We report that adrenomedullin (AM) immunoreactivity is present at high levels throughout the apical ectodermal ridge (AER) of the chick limb bud as the AER is directing the outgrowth and patterning of underlying limb mesoderm. Immunostaining is particularly strong along the surfaces of the contiguous cells of the AER. AM immunoreactivity attenuates as the AER regresses and is absent from the distal apical ectoderm of stage 20 limbless mutant limb buds which fail to develop an AER. To explore the possible role of AM in AER activity, we examined the effect of exogenous AM and an AM inhibitor on the in vitro morphogenesis of limb mesoderm, cultured in the presence and absence of the AER. Although exogenous AM cannot substitute of the AER in promoting outgrowth of limb mesoderm in vitro, a specific AM antagonist, AM(22-52), impairs the outgrowth and proliferation of limb mesoderm cultured in the presence of the AER. This is consistent with the possibility that inhibition of endogenous AM activity in the AER impairs the ability of the AER to promote limb morphogenesis. Taken together, these studies suggest that an AM-like mol. may function in an autocrine fashion to regulate some aspect of AER activity.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:708020 HCAPLUS Full-text
DOCUMENT NUMBER: 138:202507
TITLE: The effects of adrenomedullin overexpression in breast tumor cells
AUTHOR(S): Martinez, Alfredo; Vos, Michele; Guedez, Liliana; Kaur, Gurmeet; Chen, Zhong; Garayoa, Mercedes; Pio, Ruben; Moody, Terry; Stetler-Stevenson, William G.; Kleinman, Hynda K.; Cuttitta, Frank
CORPORATE SOURCE: Cell and Cancer Biology Branch and Vascular Biology Faculty, National Cancer Institute, National Institutes of Health (NIH), Bethesda, MD, 20892, USA
SOURCE: Journal of the National Cancer Institute (2002), 94(16), 1226-1237
CODEN: JNCIEQ; ISSN: 0027-8874

PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin is a secreted peptide hormone with multiple activities. Several reports have indicated that adrenomedullin may be involved in tumor survival, but this was not directly shown. Here the authors evaluate the in vitro and in vivo effects of adrenomedullin overexpression in human breast cancer cells. The human breast cancer cell lines T47D and MCF7, both of which express low basal levels of adrenomedullin, were stably transfected with an expression construct that contained the coding region of the human adrenomedullin gene or with empty expression vector. Properties of the transfected cells were assessed by proliferation and apoptosis assays, in vitro and in vivo angiogenesis assays, cell migration expts., and xenograft implants. The effect of synthetic adrenomedullin on human ovarian (ECV) cancer cell motility was also tested. Western blot anal. was used to compare expression levels of several genes whose products are associated with cell growth and regulation of apoptosis. T47D and MCF7 cells transfected with the adrenomedullin construct both expressed high levels of adrenomedullin mRNA and protein. Compared with cells transfected with empty vector, cells that overexpressed adrenomedullin displayed a more pleiotropic morphol., an increased angiogenic potential both in vitro and in vivo, and less apoptosis after serum deprivation. T47D and MCF7 cells did not display measurable motility, but ECV ovarian cancer cells treated with synthetic adrenomedullin were more motile than saline-treated ECV cells. Adrenomedullin-overexpressing T47D cells had higher levels of proteins involved in oncogenic signal transduction pathways (such as Ras, Raf, PKC, and MAPKp49) and lower levels of pro-apoptotic proteins (such as Bax, Bid, and caspase 8) than T47D cells transfected with empty vector. In a preliminary in vivo experiment, 3 of 10 nude mice injected with adrenomedullin-overexpressing T47D cells developed xenograft tumors, whereas none of the 10 nude mice injected with cells carrying the empty plasmid developed tumors. These results further support the role of adrenomedullin as a survival factor for tumors. Development of physiol. efficient inhibitors of adrenomedullin may prove useful in the clin. management of cancer.
OS.CITING REF COUNT: 47 THERE ARE 47 CAPLUS RECORDS THAT CITE THIS RECORD (49 CITINGS)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:419441 HCAPLUS Full-text
DOCUMENT NUMBER: 137:58010
TITLE: Adrenomedullin in mammalian and human skin glands including the mammary gland
AUTHOR(S): Welsch, Ulrich; Unterberger, Pia; Hofter, Eugen; Cuttitta, Frank; Martinez, Alfredo
CORPORATE SOURCE: Department of Anatomy, Chair II, University of Munich, Munich, Germany
SOURCE: Acta Histochemica (2002), 104(1), 65-72
CODEN: AHISA9; ISSN: 0065-1281
PUBLISHER: Urban & Fischer Verlag GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin was localized immunohistochem. in a variety of skin glands of humans, elephants, and impalas: apocrine scent glands, eccrine sweat glands, holocrine glands, and mammary glands. In the apocrine glands expression of adrenomedullin varied with respect to staining intensity and intracellular localization. In general, glands which appeared to be actively secreting were more strongly stained than quiescent glands. However, within a single glandular tubule, individual cells differed considerably in the staining intensity of adrenomedullin. Adrenomedullin was present in both non-lactating and lactating mammary secretory epithelia, both ducts and alveoli reacted pos. In human mammary glands displaying apocrine metaplasia, the apical protrusions were strongly pos.

Furthermore, pos. immunostaining was found in endothelium and often in smooth muscle cells of small arteries and veins and in mast cells as well. Many of the adrenomedullin-pos. epithelial cells were most strongly stained in the area of the Golgi apparatus, the cellular apex and particularly close to the basal side of the cell membrane. This pattern suggests packaging of adrenomedullin into secretory granules and secretion both at the apex of cells and at their basis. The first form of secretion suggests exocrine secretion, the latter form endocrine secretion of adrenomedullin. A possible hormonal function is in line with basally located electron dense small secretory granules, which have been found by electron microscopy in the glandular epithelia studied. OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:409606 HCAPLUS Full-text
DOCUMENT NUMBER: 137:230034
TITLE: Adrenomedullin functions as an important tumor survival factor in human carcinogenesis
AUTHOR(S): Cuttitta, Frank; Pio, Ruben; Garayoa, Mercedes; Zudaire, Enrique; Julian, Miguel; Elsasser, Ted H.; Montuenga, Luis M.; Martinez, Alfredo
CORPORATE SOURCE: Cell and Cancer Biology Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Microscopy Research and Technique (2002), 57(2), 110-119
CODEN: MRTEEO; ISSN: 1059-910X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a pluripotent regulatory peptide initially isolated from a human pheochromocytoma (adrenal tumor) and subsequently shown to play a critical role in cancer cell division, tumor neovascularization, and circumvention of programmed cell death, thus it is an important tumor cell survival factor underlying human carcinogenesis. A variety of neural and epithelial cancers have been shown to produce abundant amts. of AM. Recent findings have implicated elevation of serum AM with the onset of malignant expression. In addition, patients with tumors producing high levels of this peptide have a poor prognostic clin. outcome. Given that most human epithelial cancers display a microenvironment of reduced oxygen tension, it is interesting to note that AM and several of its receptors are upregulated during hypoxic insult. The existence of such a regulatory pathway has been implicated as the basis for the overexpression of AM/AM-R in human malignancies, thereby generating a subsequent autocrine/paracrine growth advantage for the tumor cell. Furthermore, AM has been implicated as a potential immune suppressor substance, inhibiting macrophage function and acting as a newly identified neg. regulator of the complement cascade, protective properties which may help cancer cells to circumvent immune surveillance. Hence, AM's traditional participation in normal physiol. (cited elsewhere in this issue) can be extended to a primary player in human carcinogenesis and may have clin. relevance as a biol. target for the intervention of tumor progression.
OS.CITING REF COUNT: 43 THERE ARE 43 CAPLUS RECORDS THAT CITE THIS RECORD (43 CITINGS)
REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:409602 HCAPLUS Full-text
DOCUMENT NUMBER: 137:41826

TITLE: Adrenomedullin in the central nervous system
AUTHOR(S): Serrano, J.; Alonso, D.; Fernandez, A. P.; Encinas, J. M.; Lopez, J. C.; Castro-Blanco, S.; Fernandez-Vizarra, P.; Richart, A.; Santacana, M.; Uttenthal, L. O.; Bentura, M. L.; Martinez-Murillo, R.; Martinez, A.; Cuttitta, F.; Rodrigo, J.
CORPORATE SOURCE: Department of Neuroanatomy and Cell Biology, Instituto Cajal, CSIC, Madrid, E-28002, Spain
SOURCE: Microscopy Research and Technique (2002), 57(2), 76-90
CODEN: MRTEEO; ISSN: 1059-910X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a novel vasodilator peptide first purified from human pheochromocytoma by tracing its capacity to stimulate cAMP production in platelets. AM immunoreactivity is widely distributed in the central nervous system (CNS) and in the rat has been demonstrated by immunohistochem. techniques to be present in many neurons throughout the brain and spinal cord, as well as in some vascular endothelial cells and perivascular glial cells. Electron microscopy shows that the immunoreactivity is located mainly in the neuronal cytoplasm, but also occurs in the cell nucleus in some cells of the caudate putamen and olfactory tubercle. Biochem. analyses suggest that higher mol. forms, presumably precursor forms, may predominate over fully processed AM in some brain areas. The expression of AM immunoreactivity is increased in cortical neurons, endothelial cells, and perivascular processes after a simulation of ischemia by oxygen and glucose deprivation. Immunohistochem., electrophysiol., and pharmacol. studies suggest that AM in the CNS can act as a neurotransmitter, neuromodulator, or neurohormone, or as a cytoprotective factor in ischemic/hypoxic conditions, in addition to its vasodilator role.
OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:346412 HCAPLUS Full-text
DOCUMENT NUMBER: 137:88506
TITLE: Identification, characterization, and physiological actions of factor H as an adrenomedullin binding protein present in human plasma
AUTHOR(S): Pio, Ruben; Elsasser, Ted H.; Martinez, Alfredo; Cuttitta, Frank
CORPORATE SOURCE: Department of Biochemistry and Carcinogenesis Unit, University of Navarra, Pamplona, 31080, Spain
SOURCE: Microscopy Research and Technique (2002), 57(1), 23-27
CODEN: MRTEEO; ISSN: 1059-910X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. A recently discovered adrenomedullin binding protein has been characterized as complement factor H, an important regulator of the complement cascade. This review will describe the evidence that led to the identification of factor H as an adrenomedullin binding protein and will address the implications that such binding has in the RIA of AM in plasma. We will also describe the possible physiol. implications of AM binding: namely, factor H suppresses the antimicrobial activity of AM, enhances AM-mediated induction of cyclic-AMP in rat fibroblasts, and augments the AM-mediated growth of a human cancer cell line. These initial studies suggest that factor H may be an important factor in the regulation of AM physiol. The elucidation of the mechanisms that modulate AM activity will be necessary for the understanding of the role of AM in normal

and pathol. conditions.
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:274143 HCAPLUS Full-text
DOCUMENT NUMBER: 136:380234
TITLE: Adrenomedullin, pancreatic physiology and diabetes
AUTHOR(S): Zudaire, E.; Cuttitta, F.; Martinez, A.
CORPORATE SOURCE: Department of Cell and Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Recent Research Developments in Endocrinology (2001), 2(Pt. 1), 37-54
CODEN: RRDEBU
PUBLISHER: Transworld Research Network
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a regulatory peptide ubiquitously expressed throughout the human body, that is implied in many physiol. processes. AM is expressed by the pancreatic polypeptide (PP)-containing cells in the periphery of the islets of Langerhans, while its putative receptors are found only in β-cells in the core of the islets. AM inhibits insulin secretion, presumably by a paracrine mode of action, and as a consequence elevates glycemia. New data have shown that the recently characterized AM binding protein, complement factor H, is expressed in the pancreatic insulin producing cells. Interestingly, the addition of factor H to freshly isolated islets, in the presence of AM, produces a dose-dependent further reduction of insulin secretion. Clin. data have shown that AM is elevated in several pancreatic disorders such as diabetes and insulinoma. In diabetes, AM correlates with the severity of the disease and it is specially elevated in patients with addnl. vascular complications such as nephropathy and angiopathy. In recent onset type 2 diabetes, a subpopulation of patients shows extremely high AM levels, suggesting the possible role of AM as a potential causal agent of the disorder in this subset of patients. Supporting this hypothesis, animal diabetic models have shown that treatment with a monoclonal antibody against AM dramatically reduced the hyperglycemia and the injection of synthetic AM worsened the condition. Collectively, all these findings support an implication of AM in normal and pathol. pancreatic physiol. New therapeutic approaches are envisioned using specific AM antagonists as a putative mechanism for controlling insulin/glucose disorders and eventually managing diabetes.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 145 THERE ARE 145 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:232685 HCAPLUS Full-text
DOCUMENT NUMBER: 136:399863
TITLE: Adrenomedullin expression is up-regulated by ischemia-reperfusion in the cerebral cortex of the adult rat
AUTHOR(S): Serrano, J.; Alonso, D.; Encinas, J. M.; Lopez, J. C.; Fernandez, A. P.; Castro-Blanco, S.; Fernandez-Vizarra, P.; Richart, A.; Bentura, M. L.; Santacana, M.; Uttenthal, L. O.; Cuttitta, F.; Rodrigo, J.; Martinez, A.
CORPORATE SOURCE: Department of Neuroanatomy and Cell Biology, Instituto

Cajal, CSIC, Madrid, E-28002, Spain
SOURCE: Neuroscience (Oxford, United Kingdom) (2002), 109(4), 717-731
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Changes in the pattern of adrenomedullin expression in the rat cerebral cortex after ischemia-reperfusion were studied by light and electron microscopic immunohistochem. using a specific antibody against human adrenomedullin (22-52). Animals were subjected to 30 min of oxygen and glucose deprivation in a perfusion model simulating global cerebral ischemia, and the cerebral cortex was studied after 0, 2, 4, 6, 8, 10 or 12 h of reperfusion. Adrenomedullin immunoreactivity was elevated in certain neuronal structures after 6-12 h of reperfusion as compared with controls. Under these conditions, numerous large pyramidal neurons and some small neurons were intensely stained in all cortical layers. The number of immunoreactive pre- and post-synaptic structures increased with the reperfusion time. Neurons immunoreactive for adrenomedullin presented a normal morphol. whereas non-immunoreactive neurons were clearly damaged, suggesting a potential cell-specific protective role for adrenomedullin. The number and intensity of immunoreactive endothelial cells were also progressively elevated as the reperfusion time increased. In addition, the perivascular processes of glial cells and/or pericytes followed a similar pattern, suggesting that adrenomedullin may act as a vasodilator in the cerebrocortical circulation. In summary, adrenomedullin expression is elevated after the ischemic insult and seems to be part of CNS response mechanism to hypoxic injury.
OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:918711 HCAPLUS Full-text
DOCUMENT NUMBER: 136:214377
TITLE: Cancer and diabetes: two pathological conditions in which adrenomedullin may be involved
AUTHOR(S): Pio, Ruben; Martinez, Alfredo; Cuttitta, Frank
CORPORATE SOURCE: Department of Biochemistry and Department of Histology and Pathology, School of Medicine, University of Navarra, Pamplona, 31080, Spain
SOURCE: Peptides (New York, NY, United States) (2001), 22(11), 1719-1729
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Adrenomedullin (AM) is a regulatory peptide involved in several physiol. processes. Among them, AM has been implicated in the regulation of growth, both with mitogenic and antiproliferative activities on normal cells. AM is widely expressed during embryogenesis and may have a significant role in the proliferation and differentiation processes associated with development. AM is also expressed by cancer cell lines and tumors and has been implicated in the growth of malignant cells. Some addnl. activities associated with AM (antiapoptotic capabilities, angiogenic potential, and upregulation in hypoxic conditions), together with its wide distribution in cancer, suggest that AM may be an important factor in carcinogenesis. Besides its implication in growth, embryogenesis and tumor biol., AM is also involved in pancreatic regulation and diabetes. AM regulates insulin secretion and is overexpressed in the plasma of diabetic patients. Several findings indicate that AM may participate in the pathogenesis and/or clin. complications of this disease. OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS

RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:675637 HCAPLUS Full-text
DOCUMENT NUMBER: 135:339626
TITLE: Expression of the adrenomedullin binding protein, complement factor H, in the pancreas and its physiological impact on insulin secretion
AUTHOR(S): Martinez, A.; Pio, R.; Lopez, J.; Cuttitta, F.
CORPORATE SOURCE: Department of Cell and Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Endocrinology (2001), 170(3), 503-511
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) is a ubiquitous peptide hormone which, among other functional roles, reduces insulin secretion in the pancreas. Recently we have described the interaction between AM and the complement regulator protein factor H, which results in mutual modulation of their resp. functions. Here we identify the expression of factor H in the β cells of the rat pancreatic islets by immunohistochem. and multiple immunofluorescence followed by confocal microscopy. In addition, double immunogold staining under the electron microscope showed coexistence of insulin and factor H immunoreactivities within the same secretory granules; interestingly, factor H staining was found in the electron-lucent haloes whereas the insulin antibody labeled preferentially the dense cores. The existence of factor H mRNA in the pancreas was confirmed by RT-PCR and in situ hybridization. The function of factor H in the pancreas was investigated with an insulin secretion assay. Addition of factor H to freshly isolated islets in the presence of AM resulted in a further reduction in insulin secretion with a concomitant elevation of cAMP, suggesting that factor H increases AM function in glucose homeostasis. The expression of factor H in the pancreas may play other important roles such as protection against complement-mediated cell lysis.
OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:634874 HCAPLUS Full-text
DOCUMENT NUMBER: 136:227770
TITLE: Alternative splicing of the proadrenomedullin gene results in differential expression of gene products
AUTHOR(S): Martinez, A.; Hodge, D. L.; Garayoa, M.; Young, H. A.; Cuttitta, F.
CORPORATE SOURCE: Department of Cell and Cancer Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Molecular Endocrinology (2001), 27(1), 31-41
CODEN: JMLEEI; ISSN: 0952-5041
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The adrenomedullin (AM) gene codifies for two bioactive peptides, AM and proAM N-terminal 20 peptide (PAMP). We have found two forms of the AM mRNA. Form A is devoid of introns and results in a prohormone containing both peptides. Form B retains the third intron, which introduces a premature stop codon, producing a shorter prohormone with only PAMP. Tissues with a higher B/A ratio were more immunoreactive for PAMP than for AM. The form B message was found in the cytoplasmic compartment, thus excluding that the longer message was a result of contaminating nuclear mRNA. Form B was found in cells that express PAMP but not AM. MRNA expression in a variety of cell lines was investigated by RNase protection assay and form B was found in significant amts. in two of them. Treatments that modify AM expression, such as exposure to hypoxia, were shown to change the B/A ratio and the relative secretion of AM and PAMP, indicating that the splicing mechanism for AM can be modulated and is physiol. relevant. Anal. of the sequence of the third intron and the fourth exon of the AM gene found motifs compatible with a highly regulated alternative splicing mechanism.

OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:318683 HCAPLUS Full-text

DOCUMENT NUMBER: 135:91272

TITLE: Complement factor H is a serum-binding protein for adrenomedullin, and the resulting complex modulates the bioactivities of both partners

AUTHOR(S): Pio, Ruben; Martinez, Alfredo; Unsworth, Edward J.; Kowalak, Jeffrey A.; Bengoechea, Jose A.; Zipfel, Peter F.; Elsasser, Ted H.; Cuttitta, Frank

CORPORATE SOURCE: Department of Cell and Cancer Biology, NCI, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Journal of Biological Chemistry (2001), 276(15), 12292-12300
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Adrenomedullin (AM) is an important regulatory peptide involved in both physiol. and pathol. states. The authors have previously demonstrated the existence of a specific AM-binding protein (AMBP-1) in human plasma. Here, they developed a nonradioactive ligand blotting assay, which, together with HPLC/SDS-PAGE purification techniques, allowed them to isolate AMBP-1 to homogeneity. The purified protein was identified as human complement factor H. The authors show that AM/factor H interaction interferes with the established methodol. for quantification of circulating AM. The authors' data suggest that this routine procedure does not take into account the AM bound to its binding protein. In addition, the authors show that factor H affects AM in vitro functions. It enhances AM-mediated induction of cAMP in fibroblasts, augments the AM-mediated growth of a cancer cell line, and suppresses the bactericidal capability of AM on Escherichia coli. Reciprocally, AM influences the complement regulatory function of factor H by enhancing the cleavage of C3b via factor I. Thus, the authors report on a potentially new regulatory mechanism of AM biol., the influence of factor H on RIA quantification of AM, and the possible involvement of AM as a regulator of the complement cascade.

OS.CITING REF COUNT: 93 THERE ARE 93 CAPLUS RECORDS THAT CITE THIS RECORD (93 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:275934 HCAPLUS Full-text
DOCUMENT NUMBER: 135:74165
TITLE: Distribution of adrenomedullin-like immunoreactivity in the central nervous system of the frog
AUTHOR(S): Munoz, M.; Martinez, A.; Cuttitta, F.; Gonzalez, A.
CORPORATE SOURCE: Faculty of Biology, Department of Cell Biology, University Complutense, Madrid, 28040, Spain
SOURCE: Journal of Chemical Neuroanatomy (2001), 21(2), 105-123
CODEN: JCNAEE; ISSN: 0891-0618
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adrenomedullin (AM) is a recently discovered peptide widely distributed in the mammalian brain. By using an antiserum specific for human AM, the authors have analyzed the localization of AM-like immunoreactivity in the brain and spinal cord of the anuran amphibian Rana perezi. Cell bodies immunoreactive (AMi) for AM were located in the dorsal, lateral and medial pallial regions, diagonal band of Broca, medial septum, and above and rostral to the anterior commissure. A large population of AMi neurons was located in the anterior preoptic area, suprachiasmatic nucleus and in the infundibular hypothalamus. The processes of these latter cells are part of the hypothalamo-hypophysial pathway to the neural and intermediate lobes. Labeled cells were observed in the pretectal region, posterior tubercle and the mesencephalic anteroventral tegmental nucleus. Strikingly, Purkinje cells in the cerebellum also showed AM immunoreactivity, albeit not all of these cells were equally stained. Addnl. cells were located in the parabrachial region, principal trigeminal sensory nucleus, reticular nuclei medius and inferior, and the intermediolateral gray of the spinal cord. Immunolabeled fibers were widespread throughout the brain and spinal cord of the frog. They were particularly abundant in the medial amygdala, hypothalamus, mesencephalic tectum, periventricular gray and spinal cord. The distribution pattern of AM-like immunoreactivity in the brain of the frog is very selective and does not correspond with the pattern observed for any other transmitter or neuroactive mol. The wide distribution of this peptide strongly suggests that it may play a significant role in the multiple neuronal functions in the amphibian brain.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:186032 HCAPLUS Full-text
DOCUMENT NUMBER: 134:217592
TITLE: Determination of AM-binding proteins and the association of adrenomedullin (AM) therewith
INVENTOR(S): Cuttitta, Frank; Elsasser, Ted H.; Martinez, Alfredo; Pio, Ruben
PATENT ASSIGNEE(S): Government of the United States of America as represented by the Secretary, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001018550	A2	20010315	WO 2000-US24722	20000908 <--
WO 2001018550	A3	20010802		
WO 2001018550	A9	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383419	A1	20010315	CA 2000-2383419	20000908 <--
AU 2000073622	A	20010410	AU 2000-73622	20000908 <--
AU 774725	B2	20040708		
EP 1214600	A2	20020619	EP 2000-961705	20000908 <--
EP 1214600	B1	20051221		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 313802	T	20060115	AT 2000-961705	20000908 <--
PT 1214600	E	20060531	PT 2000-961705	20000908 <--
ES 2254220	T3	20060616	ES 2000-961705	20000908 <--
US 20070025915	A1	20070201	US 2006-530411	20060908 <--
US 20090053734	A1	20090226	US 2008-236418	20080923 <--
PRIORITY APPLN. INFO.:			US 1999-153397P P	19990910 <--
			WO 2000-US24722 W	20000908 <--
			US 2002-70853 B1	20020826 <--
			US 2006-530411 A3	20060908

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for the isolation, identification, and purification of adrenomedullin (AM)-binding proteins. Also, provided are methods for utilizing the purified AM-binding proteins, or functional portions thereof, to diagnose, treat, and monitor AM-related diseases, for example, diseases or disorders associated with abnormally elevated AM levels. In addition, the present invention provides a newly identified complex between AM and a specific AM-binding protein 1 (AMBP-1); which has been isolated and identified herein as factor H (fH). The invention also provides AM/AMBP complexes, particularly AM/fH complexes, and antibodies specifically reactive with these complexes. Further provided are methods for identifying and purifying complexes of AM and an AM binding protein using anti-AM/fH antibodies, and methods for treating conditions such as cancer or diabetes utilizing compns. comprising these antibodies. The present invention addnl. provides methods for identifying antagonists agents that inhibit the function of AM, factor H, or the AM/factor H complex. The invention also provides methods for treating conditions such as cancer or diabetes using these antagonist agents. OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD

(4 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:24221 HCAPLUS Full-text

DOCUMENT NUMBER: 134:110919

TITLE: Presence of immunoreactive adrenomedullin in human and bovine milk

AUTHOR(S): Pioa, R.; Martinez, A.; Elsasser, T. H.; Cuttitta, F.

CORPORATE SOURCE: Department of Cell and Cancer Biology, National Cancer

Institute, NIH, Bethesda, MD, 20892, USA
SOURCE: Peptides (New York) (2000), 21(12), 1859-1863
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We examined by RIA the presence of immunoreactive adrenomedullin (ir-AM) in human and bovine milk. Milk samples displaced 125I-AM from the AM-antiserum in parallel to the standard curve. RP-HPLC revealed a main immunoreactive peak eluting as synthetic AM. Concns. in human milk ranged between 140 and 404 pg/mL. In cow, the levels of AM were 73.5 pg/mL. Bovine milk products had AM levels similar to those found in fresh bovine milk. Human milk had growth promoting activity on the human intestinal cell line Int-407 that could be partially blocked with an anti-AM antibody.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:521347 HCAPLUS Full-text
DOCUMENT NUMBER: 133:220943
TITLE: Hypoxia-inducible factor-1 (HIF-1) up-regulates adrenomedullin expression in human tumor cell lines during oxygen deprivation: a possible promotion mechanism of carcinogenesis
AUTHOR(S): Garayoa, Mercedes; Martinez, Alfredo; Lee, Sunmin; Pio, Ruben; An, Won G.; Neckers, Len; Trepel, Jane; Montuenga, Luis M.; Ryan, Heather; Johnson, Randall; Gassmann, Max; Cuttitta, Frank
CORPORATE SOURCE: Department of Cell and Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Molecular Endocrinology (2000), 14(6), 848-862
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Little is known about the mol. mechanisms that control adrenomedullin (AM) production in human cancers. The authors demonstrate here that the expression of AM mRNA in a variety of human tumor cell lines is highly induced in a time-dependent manner by reduced oxygen tension (1% O2) or exposure to hypoxia mimetics such as desferrioxamine mesylate (DFX) or CoCl2. This AM expression seems to be under hypoxia-inducible factor-1 (HIF-1) transcriptional regulation, since HIF-1α and HIF-1β knockout mouse cell lines had an ablated or greatly reduced hypoxia AM mRNA induction. Similarly, inhibition or enhancement of HIF-1 activity in human tumor cells showed an analogous modulation of AM mRNA. Under hypoxic conditions, immunohistochem. anal. of tumor cell lines revealed elevated levels of AM and HIF-1α as compared with normoxia, and the authors also found an increase of immunoreactive AM in the conditioned medium of tumor cells analyzed by RIA. AM mRNA stabilization was shown to be partially responsible for the hypoxic up-regulated expression of AM. In addition, the authors have identified several putative hypoxia response elements (HREs) in the human AM gene, and reporter studies with selected HREs were capable of enhancing luciferase expression after exposure to DFX. Furthermore, transient co-expression of HIF-1α resulted in an augmented transactivation of the reporter gene after DFX treatment. Given that most solid human tumors have focal hypoxic areas and that AM functions as a mitogen, angiogenic factor, and apoptosis-survival factor, the authors' findings implicate the HIF-1/AM link as a possible promotion mechanism of carcinogenesis.
OS.CITING REF COUNT: 132 THERE ARE 132 CAPLUS RECORDS THAT CITE THIS RECORD (132 CITINGS)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 23 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:443779 HCAPLUS Full-text
DOCUMENT NUMBER: 133:145366
TITLE: Expression of proadrenomedullin derived peptides in the mammalian pituitary: co-localization of follicle stimulating hormone and proadrenomedullin N-20 terminal peptide-like peptide in the same secretory granules of the gonadotropes
AUTHOR(S): Montuenga, L. M.; Burrell, M. A.; Garayoa, M.; Llopiz, D.; Vos, M.; Moody, T.; Garcia-Ros, D.; Martinez, A.; Villaro, A. C.; Elsasser, T.; Cuttitta, F.
CORPORATE SOURCE: Department of Histology and Pathology, School of Medicine, University of Navarra, Pamplona, 31080, Spain
SOURCE: Journal of Neuroendocrinology (2000), 12(7), 607-617
CODEN: JOUNE2; ISSN: 0953-8194
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Expression of proadrenomedullin-derived peptides in the rat, cow and human pituitary was studied by a variety of techniques. Immunocytochem. detection showed a widespread expression of adrenomedullin peptide in the adenohypophysis and the neural lobe, with low expression in the intermediate pituitary. Proadrenomedullin N-20 terminal peptide (PAMP)-immunoreactivity was also present in the anterior pituitary but showed a more marked heterogeneous distribution, with cells going from very strong to neg. immunostaining. Lower levels of PAMP were found in the neural lobe. Interestingly, the distribution of adrenomedullin and PAMP immunoreactivity in the anterior pituitary did not completely overlap. In the present study, we concentrated our efforts to determine which cell type of the adenohypophysis expresses PAMP. Paraffin and semithin serial sections immunostained for PAMP and the classical pituitary hormones revealed that a subpopulation of the gonadotropes expresses high levels of PAMP-immunoreactive material. Ultrastructural anal. clearly showed PAMP-immunoreactivity in the FSH-containing large secretory granules of the gonadotropes, suggesting simultaneous secretion of PAMP and FSH by this cell type. Three mouse adenohypophysis-derived cell lines (AtT20, GH3, and αT3-1 derived from corticotropes, lacto/somatotropes and gonadotropes, resp.) were also analyzed and showed expression of both proadrenomedullin-derived peptides and their mRNA. Functional studies in these three cell lines showed that neither adrenomedullin nor PAMP was able to stimulate cAMP production in our exptl. conditions. Taken together, our results support that proadrenomedullin derived peptides are expressed in the pituitary in cell-specific and not overlapping patterns, that could be explained by differences in posttranslational processing. Our data showing costorage of PAMP and FSH in the same secretory granules open a way by which PAMP could be involved in the control of reproductive physiol. in a coordinated manner with FSH. OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 24 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:255469 HCAPLUS Full-text
DOCUMENT NUMBER: 133:217403
TITLE: Modulation of endometrial steroid receptors and growth regulatory genes by tamoxifen
AUTHOR(S): Elkas, J.; Armstrong, A.; Pohl, J.; Cuttitta, F.; Martinez, A.; Gray, K.

CORPORATE SOURCE: Department of Obstetrics and Gynecology, National Naval Medical Center, Bethesda, MD, USA
SOURCE: Obstetrics & Gynecology (New York) (2000), 95(5), 697-703
CODEN: OBGNAS; ISSN: 0029-7844
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: We investigated tamoxifen's effects on the expression of growth regulatory genes in the endometrium to identify the mechanism by which tamoxifen induces proliferation. Methods: Using immunohistochem. techniques, we analyzed 39 endometrial specimens for expression of Ki-67, lactoferrin, transforming growth factor-α, tumor necrosis factor receptor-II, adrenomedullin, estrogen receptors, and progesterone receptors. Twenty specimens were obtained from postmenopausal breast cancer patients treated with tamoxifen (20 mg/day) for at least 6 mo to include two endometrial adenocarcinoma specimens. Five secretory phase, three proliferative phase, and seven atrophic endometrial specimens were used as controls. In addition, four endometrial adenocarcinoma specimens were reviewed from patients not treated with tamoxifen. Intensity of immunostaining was quantified using digitized imaging techniques. Results: Overexpression of both estrogen receptors and progesterone receptors, and an elevated proliferative index were the most consistent effects observed in benign endometrial specimens from tamoxifen-treated patients compared with atrophic controls ($P < .003$). This staining pattern was also evident in adenocarcinomas from patients who received tamoxifen. Benign endometrium from tamoxifen-treated patients also expressed transforming growth factor-α, tumor necrosis factor receptor-II, lactoferrin, and adrenomedullin at levels comparable with those found in proliferative endometrial specimens. Conclusion: These data provide further documentation that the uterotropic effects of tamoxifen may be due, at least in part, to the induction of estrogen receptors and progesterone receptors, as well as other genes associated with the proliferative phase. Furthermore, anal. of estrogen receptors, progesterone receptors, and Ki-67 may be useful in identifying postmenopausal individuals on tamoxifen, who are at increased risk for developing endometrial cancer.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 25 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:85068 HCAPLUS Full-text
DOCUMENT NUMBER: 132:263491
TITLE: Is adrenomedullin a causal agent in some cases of type 2 diabetes?
AUTHOR(S): Martinez, A.; Elsasser, T. H.; Bhathena, S. J.; Pio, R.; Buchanan, T. A.; Macri, C. J.; Cuttitta, F.
CORPORATE SOURCE: Division of Clinical Sciences, Medicine Branch, Department of Cell and Cancer Biology, National Institutes of Health, National Cancer Institute, Bethesda, MD, USA
SOURCE: Peptides (New York) (1999), 20(12), 1471-1478
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The study of two populations with a recent onset of type 2 diabetes showed that a subset of the patients had higher levels of adrenomedullin (AM) than the rest of the diabetics. In this subset, physiol. elevations of AM might have triggered the disease in predisposed individuals. Diabetics showed higher levels of AM than healthy controls. In addition, glycemia was measured in diabetic rats after injection of saline, AM, or antiAM

antibody. AM elevated glycemia, whereas the antibody reduced circulating glucose to normal. These results suggest that manipulation of AM levels could represent a new approach in the management of diabetes for the appropriate individuals.
OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS RECORD (30 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 26 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:50411 HCAPLUS Full-text
DOCUMENT NUMBER: 132:217444
TITLE: Distribution of adrenomedullin-like immunoreactivity in the rat central nervous system by light and electron microscopy
AUTHOR(S): Serrano, J.; Uttenthal, L. O.; Martinez, A.; Fernandez, A. P.; Martinez de Velasco, J.; Alonso, D.; Bentura, M. L.; Santacana, M.; Gallardo, J. R.; Martinez-Murillo, R.; Cuttitta, F.; Rodrigo, J.
CORPORATE SOURCE: Departamento de Neuroanatomia Comparada, CSIC, Instituto Cajal, Madrid, E-28002, Spain
SOURCE: Brain Research (2000), 853(2), 245-268
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin is a peptide of marked vasodilator activity first isolated from human pheochromocytoma and subsequently demonstrated in other mammalian tissues. Using a polyclonal antiserum against human adrenomedullin-(22-52) amide and the avidin-biotin peroxidase complex technique, the authors have demonstrated by light and electron microscopy that adrenomedullin-like immunoreactivity is widely distributed in the rat central nervous system. Western blotting of exts. of different brain regions demonstrated the fully processed peptide as the major form in the cerebellum, whereas a 14-kDa mol. species and a small amount of the 18-kDa propeptide were present in other brain regions. Immunoreactive neurons and processes were found in multipolar neurons and pyramidal cells of layers IV-VI of the cerebral cortex and their apical processes, as well as in a large number of telencephalic, diencephalic, mesencephalic, pontine and medullary nuclei. Cerebellar Purkinje cells and mossy terminal nerve fibers as well as neurons of the cerebellar nuclei were immunostained, as were neurons in area 9 of the anterior horn of the spinal cord. Immunoreactivity was also found in some vascular endothelial cells and surrounding processes that probably originated from perivascular glial cells. Electron microscopy confirmed the light microscopy findings and showed the reaction product in relation to neurofilaments and the external membrane of small mitochondria. Immunoreactive terminal boutons were occasionally seen. The distribution of adrenomedullin-like immunoreactivity in the central nervous system suggests that it has a significant role in neuronal function as well as in the regulation of regional blood flow.
OS.CITING REF COUNT: 65 THERE ARE 65 CAPLUS RECORDS THAT CITE THIS RECORD (65 CITINGS)
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 27 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:4780 HCAPLUS Full-text
DOCUMENT NUMBER: 132:132599
TITLE: Coexpression of receptors for adrenomedullin, calcitonin gene-related peptide, and amylin in pancreatic β-cells
AUTHOR(S): Martinez, Alfredo; Kapas, Supriya; Miller, Mae-Jean;

Ward, Yvona; Cuttitta, Frank
CORPORATE SOURCE: Department of Cell and Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Endocrinology (2000), 141(1), 406-411
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three receptors have been characterized by their ability to bind adrenomedullin (AM): L1, RDC1, and CRLR. Immunohistochem. anal. and RT-PCR showed that all three receptors are expressed by the insulin-producing cells of the islets of Langerhans. RDC1 and CRLR in the presence of particular modifying proteins can also bind calcitonin gene-related peptide (CGRP). Such data suggest that the inhibitory effect caused by both AM and CGRP on insulin secretion is mediated by a direct interaction with the β-cell. The authors also identified receptors for amylin, the third member of the AM peptide family, in mouse insulin-secreting cells. The β-cells located closer to the periphery of the islets had a stronger immunoreactivity for the AM/CGRP receptors. This observation could be related to a paracrine mechanism, given the proximity of AM- and CGRP-secreting cells (F and δ-cells, resp.), which are located at the periphery of the islets. Interestingly, the smooth muscle cells in the pancreatic vasculature expressed only RDC1, which is in agreement with physiol. data showing that AM functions in the cardiovascular system are mainly mediated through a CGRP1 receptor. These data further implicate AM and the other components of its peptide family as important regulators of insulin release. OS.CITING
REF COUNT: 39 THERE ARE 39 CAPLUS RECORDS THAT CITE THIS RECORD (39 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 28 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1999:727837 HCAPLUS Full-text
DOCUMENT NUMBER: 132:88684
TITLE: Proadrenomedullin N-terminal 20 peptide (PAMP) immunoreactivity in vertebrate juxtaglomerular granular cells identified by both light and electron microscopy
AUTHOR(S): Lopez, J.; Cuesta, N.; Martinez, A.; Montuenga, L.; Cuttitta, F.
CORPORATE SOURCE: Department of Biology (Cell Biology Unit), Faculty of Sciences, Universidad Autonoma de Madrid, Madrid, Spain
SOURCE: General and Comparative Endocrinology (1999), 116(2), 192-203
CODEN: GCENA5; ISSN: 0016-6480
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene for adrenomedullin (AM), a multifunctional peptide hormone, is expressed in mammalian renal tissue and has been shown to stimulate renin release. The exact cell source of this peptide and its gene-related partner, proadrenomedullin N-terminal 20 peptide (PAMP), in kidney is still uncertain. In the present study the authors have identified PAMP-immunoreactive cells in the kidney of different mammalian species, including man, by light microscopy. In addition, these cells have been further studied in mouse kidney by both light and electron microscopic techniques. At the light microscopic level, PAMP immunolabeling is preferentially located in the subendothelial cells of the enlarged glomerular afferent arterioles, i.e., in the juxtaglomerular cells. However, these cells do not show immunolabeling for AM. At the electron microscopic level, the immunostaining appears inside the renin-containing secretory granules of the

juxtaglomerular cells. These results confirm the direct link between renin and the AM peptide family and provide a morphol. basis for studying the potential modulatory function of AM and PAMP in the control of renin activity. In contrast, neither AM nor PAMP immunoreactivities were detected in the kidney of nonmammalian vertebrates, other than in blood vessels of particular species, providing a new phylogenetic difference in the juxtaglomerular apparatus between mammalian and nonmammalian vertebrates. (c) 1999 Academic Press. OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 29 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1999:693580 HCAPLUS Full-text
DOCUMENT NUMBER: 132:21702
TITLE: Underlying disease stress augments plasma and tissue adrenomedullin (AM) responses to endotoxin: colocalized increases in AM and inducible nitric oxide synthase within pancreatic islets
AUTHOR(S): Elsasser, Ted H.; Sartin, James L.; Martinez, Alfredo; Kahl, Stas; Montuenga, Luis; Pio, Ruben; Fayer, Ronald; Miller, Mae Jean; Cuttitta, Frank
CORPORATE SOURCE: Agricultural Research Service, U.S. Department of Agriculture, Beltsville, MD, 20705, USA
SOURCE: Endocrinology (1999), 140(11), 5402-5411
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rapid onset metabolic impairments accompany the initiation of the acute phase response to many disease stresses, whereas more chronic metabolic perturbations may prolong the recovery period. In the present experiment the application of a mild endotoxin challenge [lipopolysaccharide (LPS)] alone or additive to a chronic subclin. parasitic infection (Sarcocystis cruzi; LPS + PI) in calves was used as a model to investigate and define a dynamic axis coordinated between adrenomedullin (AM) and nitric oxide in response to immune challenge. Plasma AM and NO2/NO3 concentration responses after LPS (0.45 μg/kg, iv) were rapid in onset and of higher magnitude and longer duration in PI + LPS calves than in those challenged with LPS alone. The post-LPS increase in plasma insulin was significantly greater in PI + LPS than in LPS; following refeeding of calves, insulin secretion was most blunted in PI + LPS calves, consistent with the inhibitory effects of NO and AM on insulin secretion. A more chronic response to the immune challenge (organ specific) was in evidence in tissues harvested 24 h after LPS challenge. Where lung and liver showed no immunostaining for inducible nitric oxide (iNOS), iNOS immunostaining was present in the pancreas, localized to islets only. The percentages of iNOS-immunopos. cells in islets were 1.7%, 21%, 6.7%, and 24% for control (C; saline infused), PI, LPS, and PI + LPS calves, resp. AM immunostaining was not evident in the liver and was present, but not differentially affected by treatment, in airway epithelium in the lung. The number of islet cells with pos. immunostaining for AM was increased in LPS, PI, and PI + LPS calves. The percentages of AM-immunopos. cells in islets were 8%, 27%, 20%, and 33% for C, PI, LPS, and PI + LPS, resp. Immunostaining for AM and iNOS was colocalized with cells pos. for pancreatic polypeptide. By triple label confocal fluorescence immunocytochem., colocalization of intense AM and iNOS immunostaining was confirmed in peripheral islet cells. A weaker, more diffuse iNOS signal was also apparent in insulin-containing cells in PI + LPS. We conclude that chronic low level infection potentiates the severity of metabolic perturbations that arise with additive sudden onset immune challenge, as can occur with bacterial toxins. These metabolic disturbances are reflected in and possibly mediated by early onset increases in plasma tumor necrosis factor-α, insulin, and AM and up-regulated iNOS activity. These acute complications rapidly progress into a more chronic state

characterized by diminished insulin response to feeding stimulus and colocalized increases in pancreatic islet AM and iNOS. The pancreatic responses in AM and iNOS may play a major role in mediating prolonged disturbances in nutrient use by tissues through their influences on temporal patterns of pancreatic hormone secretion during chronic illness.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 30 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:615945 HCAPLUS Full-text

DOCUMENT NUMBER: 131:317887

TITLE: Adrenomedullin binding protein in the plasma of multiple species: characterization by radioligand blotting

AUTHOR(S): Elsasser, Ted H.; Kahl, Stanislaw; Martinez, Alfredo; Montuenga, Luis M.; Pio, Ruben; Cuttitta, Frank

CORPORATE SOURCE: Growth Biology Laboratory (THE, SK), USDA - Agricultural Research Service, Beltsville, MD, 20705, USA

SOURCE: Endocrinology (1999), 140(10), 4908-4911
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Frequently, peptide hormones circulate in plasma associated with specific binding proteins that modify the clearance and biochem. activities of the peptide. Our exptl. approach was to use 125I-ligand blotting procedures to probe for the presence of specific adrenomedullin (AM) binding proteins (AMBPs). Plasma proteins from chick, calf, dog, goat, guinea pig, human, mouse, pig, rabbit and sheep blood were separated electrophoretically in 10% nonreducing SDS-polyacrylamide gels and transferred to nitrocellulose. Nonspecific binding of tracer was blocked on the nitrocellulose with a hydrolyzed casein matrix. Blots were probed with synthetic human 125I-AM. Autoradiogram scanning of blots revealed a mixture of 140- and/or 120- kD protein complexes that bound 125I-AM in all species tested. Binding of the ligand was specific as judged by a linear competitive displacement of the tracer binding from human, bovine and pig plasma AMBP bands with increasing concns. of nonlabeled AM in the binding buffer. A series of peptide fragments of AM representing amino- and carboxy-terminal regions of the hormone, or amylin, calcitonin gene-related peptide (CGRP), or insulin failed to displace intact 125I-AM from ligand blot bands. Bovine plasma proteins from healthy and parasitized calves with an infection-related stunting syndrome were separated electrophoretically, transferred to nitrocellulose and probed with 125I-AM; phosphoimage densitometry anal. revealed a 67% decrease in AMBP band intensity in the 120 and 140 kD proteins from infected calves. We conclude that a specific binding protein(s) for AM exists in mammalian and avian blood that might impact on the bioactivity and function of AM in health and disease.

OS.CITING REF COUNT: 47 THERE ARE 47 CAPLUS RECORDS THAT CITE THIS RECORD (47 CITINGS)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 31 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:602621 HCAPLUS Full-text

DOCUMENT NUMBER: 131:281999

TITLE: Expression of adrenomedullin and proadrenomedullin N-terminal 20 peptide in human and rat prostate

AUTHOR(S): Jimenez, Nuria; Calvo, Alfonso; Martinez, Alfredo; Rosell, David; Cuttitta, Frank; Montuenga, Luis M.
CORPORATE SOURCE: Department of Histology and Pathology, University of Navarra, Pamplona, 31080, Spain
SOURCE: Journal of Histochemistry and Cytochemistry (1999), 47(9), 1167-1177
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) and proadrenomedullin N-terminal 20 peptide (PAMP) are two recently discovered hypotensive peptides translated from the same message transcript (preproAM mRNA). In this article the authors report the presence of AM, PAMP, and their mRNA in human and rat prostate and of AM receptor mRNA in rat prostate. PreproAM mRNA was found in the epithelium of normal human and rat prostate glands by in situ hybridization. In humans, it was mainly expressed in the basal cells. In rat, its expression was higher in the ducts than in the acini of all the prostate lobes. Immunocytochem. identified a similar distribution pattern for AM compared with its mRNA but showed different locations for AM and PAMP immunoreactivity. The former was widespread in the epithelia, whereas the latter was almost exclusively found in neuroendocrine cells. In rat, Western blot anal. confirmed the presence of high levels of AM peptide in the ventral lobe and of its precursor in the ventral and dorsolateral lobes. Immunoreactivity for serotonin, chromogranin A, PAMP, and AM defined four subpopulations of prostate neuroendocrine-like cells in rat, a cell type that has not been previously described. OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS
RECORD (25 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 32 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1999:574593 HCAPLUS Full-text
DOCUMENT NUMBER: 131:320396
TITLE: Adrenomedullin in nonmammalian vertebrate pancreas: an immunocytochemical study
AUTHOR(S): Lopez, J.; Cuesta, N.; Cuttitta, F.; Martinez, A.
CORPORATE SOURCE: Department of Biology (Cell Biology Unit), Faculty of Sciences, Universidad Autonoma de Madrid, Madrid, Spain
SOURCE: General and Comparative Endocrinology (1999), 115(3), 309-322
CODEN: GCENA5; ISSN: 0016-6480
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) immunoreactive cells have been identified, by immunocytochem. methods, in the endocrine pancreas of 7 nonmammalian vertebrate species, belonging to the cartilaginous and bony fish, amphibian, reptilian, and bird classes. The frequency and distribution of the pancreatic AM cells vary among the different animals. In most species, these cells are found scattered mainly among the exocrine component, with a few present in the islet-like structures. The distribution of AM cells in both fish species and Xenopus shows an inverse pattern, since almost every AM cell is located in the islets. In addition, the colocalization of AM with other classical pancreatic peptide immunoreactivities was analyzed. In numerous cells, AM immunoreactivity did not colocalize with the other hormones, suggesting that AM-producing cells might constitute a new endocrine cell type in the pancreas of many species. Nevertheless, in other cells a species-specific pattern of colocalizations with insulin, somatostatin, glucagon, and pancreatic polypeptide was found, indicating that complex interactions among all these

hormones may occur. In conclusion, AM represents a new regulatory peptide of the endocrine nonmammalian vertebrate pancreas, which is possibly involved in the modulation of insulin secretion and other pancreatic functions. (c) 1999 Academic Press. OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 33 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:386636 HCAPLUS Full-text
DOCUMENT NUMBER: 129:198377
ORIGINAL REFERENCE NO.: 129:40167a,40170a
TITLE: Expression pattern for adrenomedullin during pancreatic development in the rat reveals a common precursor with other endocrine cell types
AUTHOR(S): Martinez, A.; Cuttitta, F.; Teitelman, G.
CORPORATE SOURCE: National Cancer Institute, Division of Clinical Sciences, Cell and Cancer Biology Department, National Institutes of Health, Room 300, Rockville, MD, 20850, USA
SOURCE: Cell and Tissue Research (1998), 293(1), 95-100
CODEN: CTSRCS; ISSN: 0302-766X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin is an α-amidated 52-amino acid peptide involved in many physiol. actions, among others the regulation of insulin secretion. Using immunohistochem. methods, the authors found that adrenomedullin immunoreactivity first appears at day 11.5 of embryonic development in the rat, coinciding with the appearance of pancreatic glucagon. The early appearance of adrenomedullin in the developing pancreas may indicate an active involvement in either the morphogenesis of the organ or its endocrine/paracrine/autocrine hormone regulation during intrauterine life. The authors also investigated the pattern of co-localizations of adrenomedullin with the other pancreatic hormones. At some point during development all the cell types express adrenomedullin, progressively evolving towards the adult pattern where only the pancreatic polypeptide cells contain a strong immunoreactivity for adrenomedullin. At this point the remaining cells of the islet are, in general, weakly stained. This sequential and time-dependent expression of adrenomedullin suggests a tight regulation similar to that observed for other modulatory substances responsible for embryonic morphogenesis. OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 34 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:252119 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266645
ORIGINAL REFERENCE NO.: 128:52667a,52670a
TITLE: Adrenomedullin
AUTHOR(S): Martinez, Alfredo; Cuttitta, Frank; Editors
CORPORATE SOURCE: Neth.
SOURCE: (1998) Publisher: (IOS Press: Amsterdam, Neth.), 391 pp.
DOCUMENT TYPE: Book
LANGUAGE: English
AB Unavailable

L16 ANSWER 35 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230503 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266636
ORIGINAL REFERENCE NO.: 128:52667a,52670a
TITLE: Distribution of adrenomedullin-like immunoreactivity in the rat central nervous system: a light and electron microscopic study
AUTHOR(S): Rodrigo, J.; Serrano, J.; Martinez de Velasco, J.; Fernandez, A. P.; Bentura, M. L.; Santacana, M.; Uttenthal, L. O.; Pedrosa, J. A.; Peinado, M. A.; Gallardo, J. R.; Martinez, Alfredo; Martinez-Murillo, R.; Cuttitta, Frank
CORPORATE SOURCE: Instituto Cajal, Madrid, E-28002, Spain
SOURCE: Adrenomedullin (1998), 289-390. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Adrenomedullin is a recently discovered peptide that was purified from pheochromocytomas tissue and has marked vasodilatory activity causing hypotension and various hemodynamic changes. Using a specific polyclonal antiserum against human adrenomedullin (22-52) and the avidin-biotin peroxidase technique, the authors have demonstrated by light and electron microscopy that cell bodies and processes containing endogenous adrenomedullin are widely distributed in all regions of the rat central nervous system. In the telencephalon immunoreactive structures were distributed in all areas of the cerebral cortex in the olfactory bulb, anterior and posterior olfactory nuclei, olfactory tubercle, caudate putamen, accumbens nucleus, septum, vertical and horizontal limbs of the diagonal band, globus pallidus, substantia innominata, hippocampus and amygdala. In the diencephalon adrenomedullin was present in both hypothalamus and thalamus. The mesencephalon contained adrenomedullin- immunoreactive neurons in the interfascicular nucleus, substantia nigra, ventral tegmental area, interfascicular nucleus, rostral linear raphe nucleus, oculomotor nucleus, Darkschewitsch and Edinger-Westphal nuclei, dorsal raphe nucleus, central gray nuclei, superior colliculus and medial geniculate nucleus. In the pons and medulla oblongata, immunoreactive neurons and processes were present in the pontine nucleus, pedunculopontine tegmental nucleus laterodorsal tegmental nucleus, mesencephalic trigeminal nucleus, locus coeruleus, medial, superior and spinal vestibular nuclei, prepositus hypoglossal nucleus, dorsal cochlear nucleus, trapezoid nucleus, superior olivary nucleus, facial nucleus, pontine reticular nucleus, reticular nuclei, oral, interpolar and caudal parts of the spinal trigeminal nucleus, nucleus of the solitary tract, motor nucleus of the vagus nerve, hypoglossal nucleus, area postrema and gracile nucleus. The cerebellum showed immunoreactivity restricted to some Purkinje cells, Golgi cells and neurons of cerebellar nuclei. The mol. layer of the cerebellum contained immunoreactive apical processes of the Purkinje cells and the granule cell layer contained immunoreactive terminal arborizations of mossy fibers. The cervical, dorsal and lumbar spinal cord contained immunoreactive neurons and processes distributed in the dorsal and anterior horns and in the intermediolateral nucleus. In addition immunoreactive perivascular glial cells and endothelial vascular cells were found in all areas of the brain. The distribution of adrenomedullin in the rat brain suggests that it may modulate the functional activity of various neurotransmitter-specific systems. The possible involvement of this peptide in regulating cerebral blood flow and in neurotransmission is discussed.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 36 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230468 HCAPLUS Full-text
DOCUMENT NUMBER: 129:2858
ORIGINAL REFERENCE NO.: 129:698h,699a
TITLE: Adrenomedullin-like immunoreactivity in the central nervous system of the frog, Rana perezi
AUTHOR(S): Munoz, M.; Zudaire, E.; Martinez, Alfredo; Cuttitta, Frank; Gonzalez, A.
CORPORATE SOURCE: Dep. Cell Biol., Faculty Biology, Univ. Complutense, Madrid, 28040, Spain
SOURCE: Adrenomedullin (1998), 267-287. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The localization of adrenomedullin-like immunoreactivity (AMi) in the brain and spinal cord of the anuran amphibian R. perezi was studied by means of an antiserum specific for human AM. Cell bodies with AMi were located in the dorsal, lateral, and medial pallial regions. Labeled cells were also found in the diagonal band of Broca, medial septum, and above and rostral the anterior commissure. Weakly stained cells were present in the anterior preoptic area. A large population of AMi neurons is located in the suprachiasmatic nucleus and in the infundibular hypothalamus. The long processes of all the latter cells are part of the hypothalamo-hypophysial pathway to the intermediate lobe. A few scattered cells were weakly immunoreactive in the thalamic lateroposterior region, the posterior tubercle and the anterior tegmental nucleus of the mesencephalon. The most strikingly AMi cells were the Purkinje cells of the cerebellum, albeit not all of these cells are equally stained. Addnl. cells were located in the parabrachial region, principal trigeminal sensory nucleus, reticular nuclei medius and inferior. In the spinal cord, from cervical to lumbar segments, scattered AMi neurons were observed, preferentially in the intermediolateral gray. AMi fibers are widespread throughout the brain and spinal cord of the frog. In the telencephalon, abundant fibers are found in the diagonal band, lateral septum and amygdaloid complex, although sparse innervation is also present in the olfactory bulbs, medial septum, nucleus accumbens, striatum and lateral pallium. The anterior preoptic areas is richly innervated with AMi fibers as also is the caudal hypothalamus. Dorsally in the diencephalon, AMi varicose fibers course lateral to the thalamic lateral and posterior nuclei and reach the habenular region. More ventrally, the ventromedial thalamic nucleus and the posterior tubercle are sparsely innervated. In the brainstem, AMi fibers and terminals define a layered arrangement in the mesencephalic tectum, while ventrally less conspicuously distributed AMi fibers are present in the torus semicircularis and anterior tegmental nuclei. In the rhombencephalon, only weakly labeled fibers were observed medially and laterally to the isthmic nucleus and, more caudally, in the descending trigeminal tract and the region of the dorsal column nucleus. Finally, in the spinal cord, numerous AMi fibers that course in the dorsolateral aspect progress medially through the dorsal horn and reach the ventral region of the dorsal gray commissure. Abundant AMi fibers course longitudinally in all funiculi although fibers in the dorsal funiculus prevail.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 37 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230432 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266325
ORIGINAL REFERENCE NO.: 128:52579a,52582a
TITLE: Adrenomedullin and regulation of gastric function
AUTHOR(S): Martinez, Vicente; Kaneko, Hiroshi; Tache, Ivette

CORPORATE SOURCE: Dep. Medicine Brain Res. Inst., Univ. California, Los Angeles, CA, 90073, USA
SOURCE: Adrenomedullin (1998), 249-266. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 106 refs., of anatomical and functional evidence showing that adrenomedullin (AM) acts in the central nervous system and the periphery to inhibit gastric function and feeding behavior and of the mechanisms through which AM action is mediated. OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 38 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230423 HCAPLUS Full-text
DOCUMENT NUMBER: 128:306390
ORIGINAL REFERENCE NO.: 128:60681a,60684a
TITLE: Adrenomedullin in non-mammalian vertebrate pancreas
AUTHOR(S): Lopez Diez del Corral, J.; Cuesta Rubio, N.
CORPORATE SOURCE: Dep. Biol., Cell Biology Univ., Faculty Sciences, Univ. Autonoma Madrid, Madrid, Spain
SOURCE: Adrenomedullin (1998), 227-248. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 116 refs. Adrenomedullin seems to be a well preserved pancreatic peptide throughout the evolution of vertebrates, since it occurs from cartilaginous fish (Elasmobranchii) to mammals. The adrenomedullin cells are located both scattered among the exocrine acinar cells, except into the shark pancreas, and associated to other endocrine cells making islets or islet-like structures. They are also related to excretory ducts, except in Xenopus and chicken pancreas.
REFERENCE COUNT: 116 THERE ARE 116 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 39 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230415 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266635
ORIGINAL REFERENCE NO.: 128:52667a,52670a
TITLE: Adrenomedullin is widely expressed throughout normal and abnormal reproductive tissues of women; evidence for cyclic regulation
AUTHOR(S): Macri, Charles; Loup, Davonne; McHale, Michael; Jacobs, Robyn; Bales, Lauren; Sundborg, Michael; Armstrong, Alicia; Gehlbach, Dan; Mitchell, Annette; Nelson, Myra; Macri, Cynthia; Miller, Mae-Jean; Martinez, Alfredo; Cuttitta, Frank; Gray, Karen
CORPORATE SOURCE: Dep. Obstetrics Gynecology, National Naval Medical Center, Uniformed Services Univ. Health Sciences, Bethesda, MD, 20814, USA
SOURCE: Adrenomedullin (1998), 207-226. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press:

Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Adrenomedullin (AM) is a recently discovered potent hypotensive peptide that is widely expressed in many cell types, and apparently has pleiotropic functions including growth regulation. Proposed roles for AM include regulation of blood flow, hormone secretion, growth regulation, antimicrobial action and other potential immune functions. The purpose of the authors' study was to determine if AM expression is a characteristic feature of the normal human female reproductive tract and whether alterations occur in various disorders of these tissue. By immunocytochem. and in situ RNA detection, AM mRNA and protein were localized throughout the reproductive tract, with notable expression in the epithelial cells, blood vessels, and inflammatory cells. When investigated, AM receptor mRNA was also localized to the same cell types that were expressing the AM ligand, which indicates the existence of an autocrine AM circuit that may regulate the function of these reproductive cells. Immunohistochem. anal. of normal uterine specimens reveals that AM proteins is expressed in many cell types. The intensity and localization of AM protein in the uterus appears to be related to the menstrual phase, with the proliferative phase endometrium showing more intense cytoplasmic staining of the glandular epithelium as compared to stromal and myometrial elements. More variable AM staining is exhibited by the endometrial glands during the secretory phase with reduced cytoplasmic staining, which is associated with evidence of AM secretion and distinct localization to the nucleus. Similarly, during the secretory phase, stromal cells displays prominent cytoplasmic and nuclear AM labeling, particularly in predecidual cells. Myometrium also exhibits cyclic variation of AM ranging from cytoplasmic localization during the proliferative phase, to nuclear staining during the secretory phase. Investigation of AM expression in endometriosis, a condition where normal-appearing endometrial glands and stroma exists in ectopic locations, reveal similar patterns of expression as observed in the endometrium, but not necessarily in synchrony with the endometrium. Furthermore, some endometriotic lesions express AM protein but little mRNA, suggesting discordant regulation of AM protein and mRNA synthesis in this disease. In contrast to the benign disease endometriosis, endometrial adenocarcinomas show striking downregulation of AM protein expression, most notably in less differentiated tumors, suggesting that AM represents a marker of differentiated glandular function. Normal glands of the normal endocervix also demonstrate prominent AM immunostaining with strikingly different cellular localization patterns. The staining patterns range from diffusely cytoplasmic, basal-lateral, to nuclear which appears to represent different stages associated with mucous differentiation. In contrast, malignant endocervical glands exhibit mostly diffuse cytoplasmic staining for AM protein, that in some cases exhibited coexisting nuclear AM immunoreactivity. Like the endometrial epithelium, the epithelium of the Fallopian tube also demonstrates cyclic regulation of AM with the most intense cytoplasmic immunostaining seen during the proliferative phase. In the ovary, many cell types shows staining for AM protein. The granulosa and thecal cells of the corpus lutea and the germinal epithelium exhibit the most distinctive staining. A range of AM immunostaining is evident in ovarian epithelial tumors that appears to be related to cell-type and degree of differentiation. AM is widely expressed throughout the utero placental unit and in fetal membranes, secreted into amniotic fluid, and present in maternal serum, indicating a distinct role of AM during pregnancy. As expected, smooth muscle and endothelial cells of blood vessels demonstrate immunoreactivity for AM in all reproductive tissues. In situ of mRNA for AM ligand and its receptor reveals that these mRNAs are consistently co-localized with AM protein within the various cell types of both normal and abnormal reproductive tissues. This supports the existence of an autocrine/paracrine AM circuit in the human reproductive tract. Although further studies are needed to clarify the physiol. and pathophysiol. role of AM, the authors' study has now clearly identified AM as a novel hormone expressed in the human female reproductive tract which undoubtedly contributes to reproductive function. The presence of AM protein in different reproductive tissues regulated by steroid and gonadotropin hormones, suggests that AM may have a pivotal role

in the cyclic hormonal regulation of the reproductive tract, possibly by acting as a cytokine mediator of cell function and/or b insuring the acquisition of an adequate blood supply. OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 40 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230368 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266324
ORIGINAL REFERENCE NO.: 128:52579a,52582a
TITLE: Adrenomedullin in the adrenal cortex and medulla. Local production, receptor expression and effects of adrenomedullin and the related peptide, PAMP
AUTHOR(S): Kapas, S.; Hinson, J. P.
CORPORATE SOURCE: Dep. Oral Pathol., St. Bartholomew's, Royal London Sch. Medicine Dentistry, London, E1 2AD, UK
SOURCE: Adrenomedullin (1998), 197-206. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 31 refs. The following topics are discussed: localization of adrenomedullin and PAMP in the adrenal gland; adrenomedullin and PAMP receptors in the adrenal gland; adrenomedullin and the regulation of adrenal vascular tone; effects of adrenomedullin on aldosterone secretion; effects of adrenomedullin on glucocorticoid secretion; effects of adrenomedullin and PAMP on catecholamine secretion by the adrenal medulla.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 41 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230362 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266323
ORIGINAL REFERENCE NO.: 128:52579a,52582a
TITLE: Adrenomedullin regulates hormone secretion
AUTHOR(S): Martinez, Alfredo; Miller, Mae Jean; Montuenga, Luis M.; Cuttitta, Frank
CORPORATE SOURCE: Cell Cancer Biol. Dep., Div. Clinical Sciences, National Cancer Inst., National Inst. Health, Rockville, MD, 20850, USA
SOURCE: Adrenomedullin (1998), 185-196. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 58 refs., of the role of adrenomedullin (AM) in the regulation of hormone secretion (including pituitary hormones, hypothalamic hormones, adrenal hormones, vascular hormones, pancreatic hormones, and renin and atriopeptin). Other topics discussed include: possible signal transduction pathways for AM; alternative AM-responsive receptors; and position of AM in the hormonal chain of regulation. OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 42 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230355 HCAPLUS Full-text
DOCUMENT NUMBER: 128:266322
ORIGINAL REFERENCE NO.: 128:52579a,52582a
TITLE: Adrenomedullin: a pluripotent peptide with growth regulatory function
AUTHOR(S): Miller, Mae Jean; Martinez, Alfredo; Montuenga, Luis M.; Garayoa, Mercedes; Moody, Terry; Unsworth, Edward; Cuttitta, Frank
CORPORATE SOURCE: Cell Cancer Biology Dep., Div. Clinical Sciences, National Cancer Inst., Rockville, MD, 20850, USA
SOURCE: Adrenomedullin (1998), 171-183. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 77 refs. The growth-related cellular processes of adrenomedullin are discussed including: growth stimulation, growth inhibition, cell differentiation, apoptosis, carcinogenesis and embryogenesis. Possible therapeutic roles for AM in controlling proliferative diseases are also discussed. OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 43 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230350 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317297
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Adrenomedullin and fluid electrolyte homeostasis
AUTHOR(S): Samson, Willis K.; Vari, Richard C.; Resch, Zachary T.; Murphy, Tonya C.
CORPORATE SOURCE: Dep. Physiol., Univ. North Dakota Sch. Medicine, Grand Forks, ND, 58202-9037, USA
SOURCE: Adrenomedullin (1998), 159-170. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 45 refs. in which the actions of adrenomedullin and PAMP on fluid and electrolyte homeostasis was discussed. Renotropic, adrenal, central nervous system and pituitary actions of adrenomedullin were all discussed.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 44 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230344 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317344
ORIGINAL REFERENCE NO.: 128:62741a,62744a
TITLE: Analysis of responses to adrenomedullin in the pulmonary vascular bed
AUTHOR(S): Nossaman, Bobby Dean; Kaye, Alan David; Champion,

Hunter C.; DeWitt, Bracken; Kadowitz, Philip J.
CORPORATE SOURCE: Dep. Anesthesiology Pharmacol., Tulane Univ. Medical Center, New Orleans, LA, 70112-2699, USA
SOURCE: Adrenomedullin (1998), 143-157. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The mechanism of action of adrenomedullin (ADM), C-terminal fragments of ADM, and calcitonin gene-related peptide (CGRP), a structurally related peptide, were investigated in the pulmonary vascular bed of the rat and cat. Under conditions of elevated tone and controlled pulmonary blood flow in the isolated blood-perfused rat lung, ADM, the 15-52 amino acid C-terminal ADM fragment (ADM15-52), and CGRP caused dose-related decrease in pulmonary arterial perfusion pressure. In contrast, the C-terminal 22-52 and 40-52 amino acid fragments had no vasodilator activity. Following administration of the nitric oxide synthase inhibitors, Nw-nitro-Larginine benzyl ester or Nw-nitro-L-arginine Me ester (L-NAME), pulmonary vasodilator responses to AdM, to ADM15-52, to CGRP, to acetylcholine and to bradykinin, were significantly decreased in the rat, whereas vasodilator responses to isoproterenol and nitroglycerin were not changed. However, in the pulmonary vascular bed of the cat, L-NAME had no significant effect on vasodilator responses to ADM in doses that decreased vasodilator responses to acetylcholine and bradykinin, but had no effect on response to isoproterenol or nitric oxide. When the relative vasodilator activity of the active peptides was compared, ADM15-52 was approx. 3-fold less potent than ADM and ADM was 3-fold less potent than CGRP in decreasing pulmonary vascular resistance in the rat lung. When vasodilator responses were compared in the rat and cat, ADM was 3-fold more potent in decreasing pulmonary vascular resistance in the cat than in the rat and vasodilator responses to ADM were independent of the intervention used to raise tone in the rat. The present data demonstrate that ADM, and ADM 15-52, have significant vasodilator activity in the pulmonary vascular bed of the rat, and that responses to ADM, ADM15-52, and CGRP are dependent upon the release of nitric oxide in the rat. These studies indicate that pulmonary vasodilator responses to the peptide are mediated by different mechanisms in the pulmonary vascular bed of the rat and cat.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 45 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230311 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317639
ORIGINAL REFERENCE NO.: 128:62829a,62832a
TITLE: Analysis of cardiovascular responses to proadrenomedullin NH2-terminal 20 peptide (PAMP) in the rat and the cat
AUTHOR(S): Champion, Hunter C.; Murphy, William A.; Coy, David H.; Kadowitz, Philip J.
CORPORATE SOURCE: Dep. Pharmacol., Tulane Univ. Sch. Medicine, New Orleans, LA, 70112, USA
SOURCE: Adrenomedullin (1998), 127-142. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Responses to human proadrenomedullin N-terminal 20 peptide (hPAMP) were investigated in the regional vascular beds of the rat and cat. HPAMP decreased systemic arterial pressure and hind-quarters perfusion pressure in both species, and hPAMP was 10-

100-fold less potent than human adrenomedullin (hADM) in decreasing systemic arterial and hindquarters perfusion pressure. Responses to hPAMP were not altered by agents that interfere with the actions of the adrenergic nervous system or by surgical denervation of the regional vascular bed. Responses to hPAMP were not altered by the nitric oxide synthase inhibitor L-NAME, the K+ ATP channel antagonist U-37883A, the cyclooxygenase inhibitor meclofenamate, or type V cGMP selective phosphodiesterase inhibitor, zaprinast. The duration of the response to hPAMP was increased significantly after administration of the type IV cAMP selective phosphodiesterase inhibitor, rolipram suggesting that vasodilator responses to PAMP are mediated by cAMP-dependent mechanism in the hindquarters vascular beds of the rat and cat. The present data suggest that vasodilator responses to hPAMP are not dependent on an inhibitory effect on the adrenergic nervous system or on the release of nitric oxide and increases in cGMP, the release of vasodilator prostaglandins, or the opening of K+ATP channels in the hindquarters vascular bed of the cat. In the rat, vasodilator responses to hPAMP in the hindquarters vascular bed were not dependent on the presence of the adrenergic nervous system and were correlated closely with the baseline level of vasoconstrictor tone in the vascular bed.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 46 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230292 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317343
ORIGINAL REFERENCE NO.: 128:62741a,62744a
TITLE: Analysis of cardiovascular actions of adrenomedullin and related peptides in the cat and rat
AUTHOR(S): Champion, Hunter C.; Murphy, William A.; Coy, David H.; McNamara, Dennis B.; Kadowitz, Philip J.
CORPORATE SOURCE: Dep. Pharmacol., Tulane Univ. Sch. Medicine, New Orleans, LA, 70112, USA
SOURCE: Adrenomedullin (1998), 103-126. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Responses to human adrenomedullin (hADM), hADM analogs, and related peptides were investigated in the regional vascular bed of the rat and cat. HADM, rADM and human calcitonin gene-related peptide (hCGRP) decreased hindlimb perfusion pressure in the cat while hAmylin was without effect. The putative ADM receptor antagonist hADM-(22-52) and the CGRP receptor antagonist hCGRP-(8-37) reduced responses to hCGRP but did not alter responses to hADM. Vasodilator responses to hADM were not altered by the nitric oxide synthase inhibitor L-NAME, the K+ ATP channel antagonist U-37883A, the cyclooxygenase inhibitor meclofenamate, or the type V cGMP selective phosphodiesterase inhibitor, zaprinast. The duration of the vasodilator response to hADM was increased significantly after administration of the type IV cAMP selective phosphodiesterase inhibitor, rolipram suggesting that vasodilator responses to hADM are mediated by a cAMP-dependent mechanism in the hindlimb vascular bed of the cat. Vasodilator responses to hADM were not altered by TEA at a time when responses to endothelium-dependent vasodilator agents were reduced significantly. The hADM analog., hADM (15-52) was similar in potency to hADM at decreasing hindlimb perfusion pressure in the cat and at decreasing systemic arterial pressure in the rat. HADM-(22-52) and hADM-(40-52) did not have vasodilator activity in the cat or vasodepressor activity in the rat. Interestingly, hADM-(15-22) and hADM-(16-31) did not change systemic arterial or hindlimb perfusion pressure in the cat, but had potent vasoconstrictor activity in the systemic vascular bed of the rat. The ring structures of hCGRP [hCGRP-(1-8)] and hAmylin [hAmylin-(1-8)] had no vasopressor activity in the rat. The vasopressor responses to hADM (15-22) and hADM-(16-31) were reduced

significantly by treatment with the alpha-receptor antagonist, phentolamine, the adrenergic depleting agent, reserpine, and after bilateral adrenalectomy. The analog of rADM, [Mpr 14]-4ADM(14-50) was more potent at decreasing when injected into the corpora cavernosum of the cat. The data presented in the present study suggest that hADM has potent vasodilator activity in the rat and cat and that the ring structure of the hADM possesses vasopressor activity in the rat that is mediated by the release of adrenal catecholamines. These data suggest that there exists marked species differences in the actions of adrenomedullin in the rat and cat. OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 47 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230269 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317296
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Adrenomedullin production in vascular cells and its function in the vascular wall
AUTHOR(S): Minamino, Naoto; Isumi, Yoshitaka; Kangawa, Kenji; Kitamura, Kazuo; Matsuo, Hisayuki
CORPORATE SOURCE: National Cardiovascular Center Res. Inst., Suita, 565, Japan
SOURCE: Adrenomedullin (1998), 79-102. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 75 refs., which discusses: adrenomedullin (AM) production in endothelial cells (EC) and vascular smooth muscle cells (VSMC); regulation of AM production in VSMC; regulation of AM production in ECs; AM gene structure and regulation of AM production in VSMC; AM as a vasorelaxant in septic shock; and possible functions of AM in the vascular wall. OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS
RECORD (20 CITINGS)
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 48 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230260 HCAPLUS Full-text
DOCUMENT NUMBER: 129:39418
ORIGINAL REFERENCE NO.: 129:8265a,8268a
TITLE: Adrenomedullin in cardiovascular and renal diseases
AUTHOR(S): Kato, Johji; Kitamura, Kazuo; Eto, Tanenao
CORPORATE SOURCE: First Dep. Internal Medicine, Miyazaki Medical Coll., Miyazaki, 889-16, Japan
SOURCE: Adrenomedullin (1998), 69-77. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth.
CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review and discussion with 33 refs. Adrenomedullin (AM), a novel hypotensive peptide isolated from a human pheochromocytoma, circulates in the human blood. The plasma concns. of AM in patients with essential hypertension or primary aldosteronism have been shown to be significantly increased in relation to the elevation of blood pressure when compared to that in normotensive controls. The plasma AM in patients with congestive heart failure was also significantly higher than in controls, and the more

severe the heart failure was, the higher was the level of plasma AM. The plasma AM was significantly correlated with pulmonary artery pressure, pulmonary capillary wedge pressure, plasma natriuretic peptide concns. and renin activity in the heart failure patients. The elevated plasma AM became lower following the treatment of the heart failure. A similar elevation of the plasma AM was seen in patients with chronic renal failure and in those with end-stage renal diseases receiving hemodialysis. Taken together with the potent vasodilator and natriuretic actions of AM, these findings suggest that AM participates in defense mechanisms acting against a further deterioration of hypertension, congestive heart failure and renal failure, though a number of questions regarding the organs or tissues secreting AM into the blood and the detailed mechanism of the elevation of plasma AM remain to be answered.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 49 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230247 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317295
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Expression of AM and PAMP in normal adult and developing mammals
AUTHOR(S): Montuenga, Luis M.; Martinez, Alfredo; Miller, Mae Jean; Garayoa, Mercedes; Elasser, Ted; Cuttitta, Frank
CORPORATE SOURCE: Cell Cancer Biol. Dep., Div. Clinical Sciences, National Cancer Inst., Rockville, MD, 20850, USA
SOURCE: Adrenomedullin (1998), 49-68. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth. CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 47 refs., of the distribution of adrenomedullin and PAMP in normal adult and developing animals. OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 50 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230244 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317294
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Adrenomedullin receptors and their genes: a family in evolution?
AUTHOR(S): Clark, Adrian J. L.; Lowe, Steven
CORPORATE SOURCE: Mol. Endocrinology Lab., Dep. Endocrinology, St. Bartholomew's Hospital, London, EC1A 7BE, UK
SOURCE: Adrenomedullin (1998), 41-48. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth. CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 19 refs., of existing knowledge of adrenomedullin receptors and identification of 2 receptors for this peptide and the physiol. relevance of these.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 51 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230237 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317293
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Structure and function of adrenomedullin and PAMP
AUTHOR(S): Kitamura, Kazuo; Kangawa, Kenji; Matsuo, Hisayuki; Eto, Tanenao
CORPORATE SOURCE: First Dep. Internal Medicine, Miyazaki Medical College, Miyazaki, 5200, Japan
SOURCE: Adrenomedullin (1998), 27-39. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth. CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 50 refs., of the structure, distribution and biol. activity of the hypotensive peptides adrenomedullin and PAMP. OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 52 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:230229 HCAPLUS Full-text
DOCUMENT NUMBER: 128:317292
ORIGINAL REFERENCE NO.: 128:62729a,62732a
TITLE: Adrenomedullin: Terra incognita
AUTHOR(S): Cuttitta, Frank; Miller, Mae Jean; Montuenga, Luis M.; Garayoa, Mercedes; Elasser, Ted; Walsh, Thomas; Unsworth, Edward; Martinez, Alfredo
CORPORATE SOURCE: Cell Cancer Biol. Dep., Div. Clinical Sciences, National Cancer Inst., Rockville, MD, 20850, USA
SOURCE: Adrenomedullin (1998), 1-26. Editor(s): Martinez, Alfredo; Cuttitta, Frank. IOS Press: Amsterdam, Neth. CODEN: 65WDAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 172 refs., of several landmark discoveries in the field of adrenomedullin research, highlighting the historical progression of events leading up to the NCI Adrenomedullin Symposium. OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 172 THERE ARE 172 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 53 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:200992 HCAPLUS Full-text
DOCUMENT NUMBER: 128:304374
ORIGINAL REFERENCE NO.: 128:60197a,60200a
TITLE: Local production and action of adrenomedullin in the rat adrenal zona glomerulosa
AUTHOR(S): Kapas, S.; Martinez, A.; Cuttitta, F.; Hinson, J. P.
CORPORATE SOURCE: Department of Oral Pathology, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, E1 2AD, UK
SOURCE: Journal of Endocrinology (1998), 156(3), 477-484
CODEN: JOENAK; ISSN: 0022-0795

PUBLISHER: Journal of Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was designed to investigate the synthesis and action of adrenomedullin in the rat adrenal gland. The results obtained from in situ hybridization and immunocytochem. studies suggest that adrenomedullin is synthesized not only in the medulla, but also within the zona glomerulosa of the rat adrenal cortex. Findings from in situ hybridization and binding studies also suggested that specific adrenomedullin receptors are expressed in the zona glomerulosa, and that low levels are present in the inner zones of the cortex. The Kd of the zona glomerulosa adrenomedullin receptor (5.5 nmol/l) suggests that it may respond to locally produced adrenomedullin rather than circulating concns. of the peptide, which are in a lower range. It was found that adrenomedullin acted on zona glomerulosa cells in vitro to stimulate aldosterone release and cAMP formation, but in this tissue did not stimulate inositol phosphate turnover. The effect of adrenomedullin on aldosterone secretion was significantly attenuated by a protein kinase A inhibitor, suggesting that cAMP mediates the effects of adrenomedullin on aldosterone secretion. Adrenomedullin did not significantly affect the response of zona glomerulosa cells to stimulation by either ACTH or angiotensin II. Adrenomedullin did not affect the release of catecholamines, either adrenaline or noradrenaline, by intact adrenal capsular tissue. These data suggest that both adrenomedullin and its specific receptor are expressed in the rat adrenal zona glomerulosa, leading to the hypothesis that adrenomedullin may have an autocrine/paracrine role in the regulation of the rat adrenal zona glomerulosa.
OS.CITING REF COUNT: 75 THERE ARE 75 CAPLUS RECORDS THAT CITE THIS RECORD (75 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 54 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:72714 HCAPLUS Full-text
DOCUMENT NUMBER: 128:203190
ORIGINAL REFERENCE NO.: 128:40138h,40139a
TITLE: Localization of adrenomedullin-like immunoreactivity in the hypothalamo-hypophysial system of amphibians
AUTHOR(S): Gonzalez, Agustin; Marin, Oscar; Sanchez-Camacho, Cristina; Jose Pena, Juan; Zudaire, Enrique; Martinez, Alfredo; Cuttitta, Frank; Munoz, Margarita
CORPORATE SOURCE: Faculty of Biology, Department. of Cell Biology, University Complutense, 28040, Madrid, Spain
SOURCE: Neuroscience Letters (1998), 242(1), 13-16
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of adrenomedullin-like immunoreactive (AMi) cell bodies and fibers in the hypothalamus and hypophysis of the amphibians Rana perezi (anuran) and Pleurodeles waltl (urodele) was examined by immunohistochem. A large population of AMi neurons was found in the suprachiasmatic nucleus of both species. Differently, AMi cells in the magnocellular nucleus of the preoptic area were only found in the urodele, whereas dispersed cells in the caudal infundibular region were exclusively present in the anuran. This different staining pattern is reflected in the hypophysis where the neural lobe is primarily immunoreactive in the urodele while the labeling in the intermediate lobe prevailed in the anuran. The results strongly suggest that, as is mammals, the AM in amphibians may play an important regulatory role in the hypothalamo-hypophysial system.
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 55 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:22761 HCAPLUS Full-text
DOCUMENT NUMBER: 128:136801
ORIGINAL REFERENCE NO.: 128:26783a,26786a
TITLE: Adrenomedullin expression in the mouse mammary gland: evidence for the mature form in milk
AUTHOR(S): Jahnke, G. D.; Miller, M.-J.; Martinez, A.; Montuenga, L.; Cuttitta, F.
CORPORATE SOURCE: Reproductive Toxicol. Workgroup, Lab. Toxicol., Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Molecular Endocrinology (1997), 19(3), 279-289
CODEN: JMLEEI; ISSN: 0952-5041
PUBLISHER: Journal of Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) is a recently identified amidated peptide produced by a variety of tissue types. The authors have investigated the involvement of AM and its receptor (AM-R) in developing mouse mammary glands and have examined what influence ovarian hormones have on AM and AM-R expression in this system. Tissues from ductal morphogenesis, virgin adult, pregnancy, and lactation stages were assessed for AM and AM-R by mol., biochem. and immunohistochem. techniques. From these studies indicated that mRNA for AM and AM-R and immunoreactivity for AM were expressed in the luminal epithelium of small and large ducts and in terminal end buds. Immunoreactive AM was identified as a cytoplasm component of ductal cells, with some cells also having nuclear staining. Western blot anal. of mammary gland tissues yielded two mol. mass species (Mr 14,000 and 18,500) of AM immunoreactivity in the mammary gland for the above developmental stages, consistent with processed intermediate and prohormone forms resp. Ovariectomy alone or followed by hormonal treatments did not alter the expression pattern for these two proteins. By Western blot, the fully processed AM form (Mr 6000) was identified in milk exts. from lactating glands. These data suggest a potential role for AM and its receptor in the maintenance of mammary gland homeostasis and suggests a potential role for AM in development of the newborn. OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS
RECORD (19 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 56 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:757972 HCAPLUS Full-text
DOCUMENT NUMBER: 128:57719
ORIGINAL REFERENCE NO.: 128:11175a,11178a
TITLE: Expression of adrenomedullin and its receptor in normal and malignant human skin: a potential pluripotent role in the integument
AUTHOR(S): Martinez, Alfredo; Elsasser, Theodore H.; Muro-Cacho, Carlos; Moody, Terry W.; Miller, Mae Jean; Macri, Charles J.; Cuttitta, Frank
CORPORATE SOURCE: Cell and Cancer Biology Department, Medicine Branch, Division of Clinical Sciences, National Cancer Inst., National Institutes of Health, Rockville, MD, 20850, USA
SOURCE: Endocrinology (1997), 138(12), 5597-5604
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Adrenomedullin (AM) is a multifunctional peptide involved in a variety of physiol. functions, including growth regulation and antimicrobial activity. We have determined by immunohistochem. and in situ hybridization that AM and its receptor are present in all the epithelial cells of the normal skin, including keratinocytes of the epidermis and hair follicles, as well as cells of the glands and secretory ducts. We also have detected AM in the sweat, by RIA. In addition, AM and its receptor were found in skin tumors of different histol. The presence of AM and its receptor in normal and neoplastic skin was confirmed by RT-PCR and Western blot anal. performed on cell exts. from human skin cell lines. Radiolabeled AM bound to specific sites in cultured cells with a Kd of 9 nM. This binding was blocked by the addition of cold AM but not by related peptides such as AM 22-52, pro-AM 20 N-terminal peptide, calcitonin gene-related peptide, calcitonin gene-related peptide 8-37, or amylin. Finally, exposure to synthetic AM resulted in an increase of thymidine intake by skin cells. These results implicate AM as a potential player in skin defense against infectious microorganisms and as a possible autocrine growth factor in normal skin physiol. and tumor development. OS.CITING REF
COUNT: 83 THERE ARE 83 CAPLUS RECORDS THAT CITE THIS RECORD (83 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 57 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:733619 HCAPLUS Full-text
DOCUMENT NUMBER: 128:33057
ORIGINAL REFERENCE NO.: 128:6461a,6464a
TITLE: Adrenomedullin binds with high affinity, elevates cyclic AMP, and stimulates c-fos mRNA in C6 glioma cells
AUTHOR(S): Moody, T. W.; Miller, M. J.; Martinez, A.; Unsworth, E.; Cuttitta, F.
CORPORATE SOURCE: Department of Cell and Cancer Biology, Medicine Branch, Division of Clinical Sciences, National Cancer Institute, Rockville, MD, 20850, USA
SOURCE: Peptides (New York) (1997), 18(8), 1111-1115
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of adrenomedullin (ADM) on C6 glioma cells were investigated. [125I]ADM bound with high affinity (Kd = 24 nM) to a single class of sites (Bmax = 36,000/cell) in C6 cells. Specific [125I]ADM binding was inhibited with high affinity by ADM (IC50 value of 10 nM) but not ADM(22-52) or pro-adrenomedullin N-terminal 20 peptide (PAMP). By RT-PCR, ADM receptors were detected in C6 cells. ADM elevated cAMP (ED50 value of 10 nM) whereas PAMP and ADM(22-52) did not. ADM stimulated transiently c-fos mRNA in a concentration-dependent manner. Monoclonal antibody G6, which neutralizes ADM, significantly inhibited C6 proliferation and decreased the ability of ADM to elevate c-fos mRNA. These data suggest that ADM is a regulatory peptide of C6 cells. OS.CITING REF
COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 58 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:238426 HCAPLUS Full-text
DOCUMENT NUMBER: 126:221081
ORIGINAL REFERENCE NO.: 126:42643a,42646a
TITLE: Adrenomedullin as a universal autocrine growth factor for tumor cells and in control of insulin

release
INVENTOR(S): Cuttitta, Frank; Martinez, Alfredo; Miller, Mae Jean; Unsworth, Edward J.; Hook, William; Walsh, Thomas; Gray, Karen; Macri, Charles; et al.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9707214	A1	19970227	WO 1996-US13286	19960816 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2229741	A1	19970227	CA 1996-2229741	19960816 <--
AU 9667765	A	19970312	AU 1996-67765	19960816 <--
AU 710662	B2	19990923		
EP 845036	A1	19980603	EP 1996-928205	19960816 <--
EP 845036	B1	19990602		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 180832	T	19990615	AT 1996-928205	19960816 <--
JP 11512087	T	19991019	JP 1997-509499	19960816 <--
US 6320022	B1	20011120	US 1998-11922	19980217 <--
US 20020055615	A1	20020509	US 2001-931700	20010816 <--
US 7101548	B2	20060905		
US 20070004630	A1	20070104	US 2006-517599	20060905 <--
US 7622272	B2	20091124		
JP 2007145850	A	20070614	JP 2006-349430	20061226 <--
JP 4077861	B2	20080423		
US 20100021469	A1	20100128	US 2009-569821	20090929 <--

PRIORITY APPLN. INFO.:			
US 1995-2514P	P	19950818	<--
US 1995-2936P	P	19950830	<--
US 1996-13172P	P	19960312	<--
JP 1997-509499	A3	19960816	<--
WO 1996-US13286	W	19960816	<--
US 1998-11922	A3	19980217	<--
US 2001-931700	A1	20010816	<--
US 2006-517599	A3	20060905	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Adrenomedullin (AM) is found in human cancer cell lines of diverse origin and functions as a universal autocrine growth factor driving neoplastic proliferation. AM peptides and AM antibodies useful in therapeutic, pharmacol. and physiol. compns. are described. Methods of diagnosis, treatment and prevention of disease using theses AM peptides and antibodies are also described. Exptl. models for use in identifying the role of AM in pancreatic physiol. are also described. Expts. using isolated rat pancreatic islets have shown that AM inhibits insulin secretion in a dose-dependent manner. The monoclonal antibody MoAb-G6, which neutralizes AM bioactivity, was shown to increase insulin release fivefold, an effect that was reversed by the addition of synthetic AM. OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD

(9 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 59 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:188613 HCAPLUS Full-text
DOCUMENT NUMBER: 126:259596
ORIGINAL REFERENCE NO.: 126:50144h,50145a
TITLE: Adrenomedullin receptor expression in human lung and in pulmonary tumors
AUTHOR(S): Martinez, Alfredo; Miller, Mae Jean; Catt, Kevin J.; Cuttitta, Frank
CORPORATE SOURCE: Division of Clinical Sciences, Biomarkers and Prevention Research Branch, National Cancer Institute, National Institutes of Health, Rockyille, MD, 20850-3300, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1997), 45(2), 159-164
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) is a multifunctional regulatory peptide that stimulates cAMP production in may target tissues and is highly expressed in the lung. Anal. of the distribution of the recently cloned AM receptor (AM-R) by nonradioactive in situ hybridization revealed abundant expression in the basal cells of the airway epithelium and Type II pneumocytes. The expression of AM-R in the two cell types involved in epithelial regeneration of the lung suggests that AM may be relevant in such functions as organ development, wound repair, and epithelial turnover. AM-Rs are also synthesized in vivo and in vitro by a variety of tumor cells that also express the ligand, suggesting the existence of an autocrine loop that may be involved in tumor growth stimulation. The present findings suggest that the AM/AM-R regulatory system plays a major role in respiratory physiol. and lung carcinogenesis and that new functions for AM remain to be identified. OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)

L16 ANSWER 60 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:3732 HCAPLUS Full-text
DOCUMENT NUMBER: 126:43146
ORIGINAL REFERENCE NO.: 126:8408h,8409a
TITLE: Expression of adrenomedullin and its receptor during embryogenesis suggests autocrine or paracrine modes of action
AUTHOR(S): Montuenga, Luis M.; Martinez, Alfredo; Miller, Mae Jean; Unsworth, Edward J.; Cuttitta, Frank
CORPORATE SOURCE: Biomarkers and Prevention Research Branch, National Cancer Institute, Rockville, MD, 20850, USA
SOURCE: Endocrinology (1997), 138(1), 440-451
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study reports the developmental patterns of expression of adrenomedullin (AM) in rat and mouse embryos. AM is a novel multifunctional peptide recently isolated from a human pheochromocytoma, which has been shown to promote growth in a variety of mammalian cell lines. We have applied several techniques to investigate the localization of both the AM peptide and its receptor throughout development. Immunocytochem. detection has been performed using different specific antibodies against

AM ant its gene-related peptide pro-AM N-terminal 20 peptide. In situ hybridization showed the localization of the mRNAs for AM and its receptor. Western blot anal. together with reverse transcription-PCR gave further support to the localization of AM and its receptor in a variety of embryonic tissues. The localization of the receptor paralleled that of AM itself, suggesting an autocrine or paracrine mode of action. The spatio-temporal pattern of expression of AM in cardiovascular, neural, and skeletal-forming tissues as well as in the main embryonic internal organs is described. The primitive placenta, especially the giant trophoblastic cells, shows high levels of AM during development. The kidney, lung, and developing tooth, in which epithelial-mesenchymal interactions are taking place, show specific patterns of AM expression. In several regions of the embryo, the patterns of AM expression correspond to the degree of differentiation. The possible involvement of AM in the control of embryonic invasion, proliferation, and differentiation is discussed.
OS.CITING REF COUNT: 129 THERE ARE 129 CAPLUS RECORDS THAT CITE THIS RECORD (129 CITINGS)

L16 ANSWER 61 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1996:711646 HCAPLUS Full-text
DOCUMENT NUMBER: 126:27251
ORIGINAL REFERENCE NO.: 126:5465a,5468a
TITLE: Detection of adrenomedullin, a hypotensive peptide, in amniotic fluid and fetal membranes
AUTHOR(S): Macri, Charles J.; Martinez, Alfredo; Moody, Terry W.; Gray, Karen D.; Miller, Jae-Jean; Gallagher, Michael; Cuttitta, Frank
CORPORATE SOURCE: National Cancer Institute, Uniformed Services University Health Sciences, Bethesda, MD, USA
SOURCE: American Journal of Obstetrics and Gynecology (1996), 175(4, Pt. 1), 906-911
CODEN: AJOGAH; ISSN: 0002-9378
PUBLISHER: Mosby-Year Book
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors' purpose was to determine whether adrenomedullin, a multifunctional regulatory peptide involved in blood flow regulation and growth stimulation and with antimicrobial activity, was a component of amniotic fluid from second-trimester human fetus and to determine the source of this peptide. A prospective descriptive study was performed on 134 patients undergoing amniocentesis after genetic counseling, ultrasonog., and informed consent. Adrenomedullin expression was determined by immunocytochem. anal., Western blot anal., reverse transcriptase-polymerase chain reaction, and in situ reverse transcriptase-polymerase chain reaction in fetal membranes and with RIA in amniotic fluid. RIA of the 134 amniotic fluid specimens revealed adrenomedullin-like immunoreactivity in all of them, ranging in concentration from 10 to 300 fmol/25 μL. Immunocytochem. anal., Western blot anal., reverse transcriptase-polymerase chain reaction, and in situ reverse transcriptase-polymerase chain reaction further established the expression of adrenomedullin protein and mRNA in fetal amniotic membranes, suggesting that this organ is the source of amniotic adrenomedullin. The authors' results clearly demonstrate the presence of adrenomedullin second-trimester human amniotic fluid and adrenomedullin mRNA and protein in amniotic membranes, suggesting that adrenomedullin is a hormone involved in the maintenance of normal pregnancy. Further studies with these mol. tools are in progress to determine the precise role of this hormone and whether adrenomedullin plays a role in the pathogenesis of various disorders of pregnancy.
OS.CITING REF COUNT: 58 THERE ARE 58 CAPLUS RECORDS THAT CITE THIS RECORD (58 CITINGS)

L16 ANSWER 62 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1996:584430 HCAPLUS Full-text
DOCUMENT NUMBER: 125:293872

ORIGINAL REFERENCE NO.: 125:54759a,54762a
TITLE: Adrenomedullin expression in human tumor cell lines. Its potential role as an autocrine growth factor
AUTHOR(S): Miller, Mae Jean; Martinez, Alfredo; Unsworth, Edward J.; Thiele, Carol J.; Moody, Terry W.; Elsasser, Theodore; Cuttitta, Frank
CORPORATE SOURCE: Biomarkers Prevention Res. Branch, National Cancer Inst., Rockville, MD, 20850, USA
SOURCE: Journal of Biological Chemistry (1996), 271(38), 23345-23351
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although adrenomedullin (AM) previously has been identified in human tumors, its role has remained elusive. Anal. by reverse transcriptase-polymerase chain reaction (RT-PCR) revealed AM mRNA in 18 of 20 human normal tissues representing major organs, and 55 of 58 (95%) malignant cell lines. Western blot and HPLC anal. showed immunoreactive Am species of 18, 14, and 6 kDa that are consistent with the precursor, intermediate product, and active peptide, resp. Immunohistochem. and in situ RT-PCR performed on paraffin-embedded tumor cell lines of various tissue origins exhibited AM cytoplasmic staining. Neutralizing monoclonal antibody to AM inhibits tumor cell growth in a concentration-dependent manner, an effect that was reversed with the addition of exogenous AM. Responding tumor cells were shown to have approx. 50,000 Am receptors per cell by Scatchard anal. with 125I-AM and expressed AM receptor mRNA by RT-PCR. The authors' data showed 36 of 48 (75%) tumor cell lines expressed AM receptor mRNA by RT-PCR assessment, all of them also expressed AM. In the presence of AM, cAMP levels were shown to increase in tumor cells. The authors' collective data demonstrate that AM and AM receptor are expressed in numerous human cancer cell lines of diverse origin and constitute a potential autocrine growth mechanism that could drive neoplastic proliferation.
OS.CITING REF COUNT: 230 THERE ARE 230 CAPLUS RECORDS THAT CITE THIS RECORD (230 CITINGS)

L16 ANSWER 63 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1996:311894 HCAPLUS Full-text
DOCUMENT NUMBER: 124:333912
ORIGINAL REFERENCE NO.: 124:61745a,61748a
TITLE: Regulation of insulin secretion and blood glucose metabolism by adrenomedullin
AUTHOR(S): Martinez, Alfredo; Weaver, Cyprian; Lopez, Jose; Bhathena, Sam J.; Elsasser, Theodore H.; Miller, Mae-Jean; Moody, Terry W.; Unsworth, Edward J.; Cuttitta, Frank
CORPORATE SOURCE: Division Clinical Sciences, National Cancer Inst., Rockville, MD, 20850, USA
SOURCE: Endocrinology (1996), 137(6), 2626-2632
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM), a recently discovered hypotensive peptide, is expressed in the endocrine pancreas of different species, as demonstrated by immunocytochem. Electron microscopic studies with double immunogold showed colocalization of AM and pancreatic polypeptide. A homogeneous expression of AM receptor was found throughout the islet using in situ hybridization. Six different insulin-producing cell lines have been analyzed by reverse transcription-PCR and showed expression of both AM and its receptor.

Two exptl. models have been used to study the effects of AM in pancreatic physiol. Anal. of isolated rat islets shows that AM inhibits insulin secretion in a dose-dependent manner. The monoclonal antibody MoAb-G6, which neutralizes AM bioactivity, was able to increase insulin release 5-fold; this effect was reversed by the addition of synthetic AM. Oral glucose tolerance tests showed that i.v. injection of AM reduces the levels of insulin in the bloodstream with a concomitant increase in circulating glucose. These studies implicate AM as a newly defined factor of the insulin regulatory system that could be involved in disorders such as diabetes and obesity.
OS.CITING REF COUNT: 118 THERE ARE 118 CAPLUS RECORDS THAT CITE THIS RECORD (119 CITINGS)

L16 ANSWER 64 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1996:178391 HCAPLUS Full-text
DOCUMENT NUMBER: 124:227311
ORIGINAL REFERENCE NO.: 124:42005a,42008a
TITLE: Adrenomedullin-like immunoreactivity in the nervous system of the starfish Marthasterias glacialis
AUTHOR(S): Martinez, A.; Unsworth, E. J.; Cuttitta, F.
CORPORATE SOURCE: Biomarkers and Prevention Research Branch, National Cancer Institute, Rockville, MD, 20850-3300, USA
SOURCE: Cell and Tissue Research (1996), 283(2), 169-72
CODEN: CTSRCS; ISSN: 0302-766X
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nervous system of the starfish Marthasterias glacialis was investigated immunocytochem. using an antiserum specific for adrenomedullin (AM), a new regulatory peptide. Immunoreactivity was only found in nerves of the basiepithelial plexus of cardiac and pyloric stomachs and pyloric caeca, while the radial nerve cords and the other digestive organs were neg. The strongest AM-like immunoreactivity was located in the current-producing areas of the cardiac stomach. The distribution of this peptide suggests different functions in echinoderms involving regulation of muscle movement and neurotransmission. The presence of an AM-like substance in echinoderms points to an early phylogenetic origin for this regulatory system. OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS RECORD (30 CITINGS)

L16 ANSWER 65 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1995:761377 HCAPLUS Full-text
DOCUMENT NUMBER: 123:166452
ORIGINAL REFERENCE NO.: 123:29647a,29650a
TITLE: Expression of adrenomedullin in normal human lung and in pulmonary tumors
AUTHOR(S): Martinez, Alfredo; Miller, Mae Jean; Unsworth, Edward J.; Siegfried, Jill M.; Cuttitta, Frank
CORPORATE SOURCE: Biomarkers Prevention Res. Branch, Div. Cancer Prevention Control, Natl. Cancer Inst., Natl. Inst. Health, Rockville, MD, 20850-3300, USA
SOURCE: Endocrinology (1995), 136(9), 4099-105
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adrenomedullin (AM) is a potent hypotensive peptide recently discovered in exts. of human pheochromocytoma. In this report evidence is presented, using reverse transcriptase-polymerase chain reaction, immunocytochem., and in situ reverse transcriptase-polymerase chain reaction, that AM is synthesized by several cell populations of the normal lung, tumor cell lines of pulmonary origin, and tumor

specimens. Among the normal cell populations of the lung, AM expression was found in the columnar epithelium, some glands, neurons of the pulmonary parasympathetic nervous system, endothelial cells, chondrocytes, alveolar macrophages, and smooth muscle cells. In tumors, AM expression was located in most of the nonsmall cell lung carcinomas and in half of the small cell lung carcinomas studied. These findings suggest that AM may play a broad role in respiratory homeostasis and lung carcinogenesis. OS.CITING REF COUNT: 163 THERE ARE 163 CAPLUS RECORDS THAT CITE THIS RECORD (163 CITINGS)

L16 ANSWER 66 OF 66 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1993:667255 HCAPLUS Full-text
DOCUMENT NUMBER: 119:267255
ORIGINAL REFERENCE NO.: 119:47737a,47740a
TITLE: Localization of amidating enzymes (PAM) in rat gastrointestinal tract
AUTHOR(S): Martinez, Alfredo; Burrell, Maria A.; Kuijk, Marjolein; Montuenga, Luis M.; Treston, Anthony; Cuttitta, Frank; Polak, Julia M.
CORPORATE SOURCE: Dep. Cytol. Histol., Univ. Navarra, Pamplona, Spain
SOURCE: Journal of Histochemistry and Cytochemistry (1993), 41(11), 1617-22
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the distribution of the two enzymes involved in post-translational C-terminal α-amidation of regulatory peptides in rat digestive tract, using immunocytochem. methods and in situ hybridization techniques. The enzymes were located in most of the fibers and neurons of the myenteric and submucous plexus throughout the entire digestive tract and in endocrine cells of the stomach and colon. Staining of reverse-face serial sections demonstrated that the enzymes in endocrine cells of the stomach co-localized with gastrin in the bottom of the gastric glands. Some gastrin-immunoreactive cells near the neck of the gland were neg. for PAM, suggesting that amidation takes place only in the more mature cells. In the colon all cells immunoreactive for glucagon and GLP1 were also pos. for peptidylglycan α-hydroxylating monooxygenase (PHM) but not for peptidyl-α-hydroxyglycine α-amidating lyase (PAL). The absence of immunoreactivity for the amidating enzymes in endocrine cells of the small intestine, known to produce C-terminally amidated peptides, suggests the existence of other amidating enzymes.
OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

```
=> d his nofile

     (FILE 'REGISTRY' ENTERED AT 12:06:13 ON 03 FEB 2010)
L1             STR
L3          119 SEA SSS FUL L1
L4             STR
L5            8 SEA SUB=L3 SSS FUL L4

     FILE 'HCAPLUS' ENTERED AT 12:28:45 ON 03 FEB 2010
L6            9 SEA ABB=ON  PLU=ON  L5
                D STAT QUE L6
                D IBIB ABS HITSTR L6 1-9
L7          233 SEA ABB=ON  PLU=ON  ("CUTTITTA F"/AU OR "CUTTITTA F F"/AU OR
                "CUTTITTA FRANCK"/AU OR "CUTTITTA FRANK"/AU OR "CUTTITTA FRANK
                C"/AU OR "CUTTITTA FRANK F JR"/AU OR "CUTTITTA FRANKLIN"/AU)
L8         1986 SEA ABB=ON  PLU=ON  ("MARTINEZ ALFREDO"/AU OR "MARTINEZ
                ALFREDO CORDOVA"/AU OR "MARTINEZ ALFREDO J"/AU OR "MARTINEZ
                ALFREDO LORENZO LUACE"/AU OR "MARTINEZ ALFREDO ORDEN"/AU) OR
                MARTINEZ A/AU OR MARTINEZ A ?/AU
L11           93 SEA ABB=ON  PLU=ON  L7 AND L8
L14           82 SEA ABB=ON  PLU=ON  L11 AND (?ADRENO? OR ?GAST?)
L15           67 SEA ABB=ON  PLU=ON  L14 AND (AY=<2003 OR PY=<2003 OR PRY=<2003
                OR PD=<OCTOBER 8, 2003)
L16           66 SEA ABB=ON  PLU=ON  L15 NOT L6
                D STAT QUE L16
                D IBIB ABS HITSTR L16 1-66

=>
```